CASE AUTH/3031/4/18

ANONYMOUS NON-CONTACTABLE HEALTH PROFESSIONAL v GILEAD

Speaker training meeting

An anonymous, non-contactable health professional alleged that a Gilead Oncology Faculty Meeting held in Frankfurt in March 2018, constituted disguised promotion of Zydelig (idelalisib). Zydelig was used in certain adult patients with either chronic lymphocytic leukaemia (CLL) or follicular lymphoma (FL).

The complainant stated that it was only after arriving that he/she found out that the premise of the meeting was to train speakers on Zydelig and for them then to go out and speak about the medicine. This was not made entirely clear beforehand. The complainant submitted that the content was not balanced medical education.

Throughout the meeting Zydelig was shown in a positive light and competitors in a negative light. The meeting revolved around Zydelig – there was no balance. Even in a statistics lecture, the worked examples were chosen to cast doubt on either competitor data, or data which could be perceived as negative for Zydelig. The complainant alleged that this disparaged competitor medicines and was clearly promotional in tone and content.

The complainant alleged that the meeting co-chair from Gilead was overtly biased in that he/she actively took part in discussions and directed the meeting in a way that one would have expected at a promotional meeting. The co-chair brought up positive aspects of Zydelig and disparaged one competitor medicine and questioned the validity of data on another. Further, he/she asked questions of the speakers so that positive Zydelig data would be discussed, even off-label data.

The complainant stated that on day 2 he/she was appalled to hear Zydelig positioned as a preventative treatment for Richter's transformation (RT) in chronic lymphocytic leukemia. There was no data to support those claims; it was all hypothesis and postulation.

Gilead appeared to accept and verbalize these hypotheses that Zydelig was an 'immuno-oncology compound which suppressed the high-risk clones' as fact, without any data to support the claims. A table used to highlight a lower rate of RT with Zydelig used data from off-label studies – this slide was freely available for delegates to download afterwards from the Gilead Oncology Faculty Portal. The complainant alleged that there was off-label data throughout the portal (which consisted of hundreds of slides).

The complainant also noted that half of the attendees were from Italy. The complainant queried whether they all went out and talked about Zydelig following the meeting, or even a substantial proportion of them. The meeting appeared to be a reasonably efficient way for Gilead to have a large contingent held captive for two days while paid speakers promoted to them.

The detailed response from Gilead is given below.

The Panel noted Gilead's explanation that the Gilead Oncology Faculty was a register of trained speakers but it queried whether the title of the meeting, Gilead Oncology Faculty meeting, fairly reflected the stated purpose of the meeting. In the Panel's view such faculties were often used to describe company convened meetings of key opinion leaders and such like. The impression given by the title of the meeting was important.

The Panel noted Gilead's submission that the meeting was an appropriate training meeting to ensure that health professionals whom the company intended to engage to speak on its behalf had a detailed understanding of the clinical dataset. When determining whether the content was appropriate the Panel considered that the overall arrangements, the therapy area and the professional status of the delegates were relevant. In the Panel's view, delegates should know at the outset and before their attendance that the meeting was a speaker training event and that they would be engaged as speakers thereafter.

The Panel noted that speaker contracts were covered by contracts with consultants. The Panel considered that in principle it was good practice when training speakers to fulfil future speaker engagements to ensure that a written agreement covered the training activity to ensure that the arrangements including the nature of the meeting, the context in which data was presented and the parties' responsibilities and relationship were clear. Such written agreements were particularly important if the material disseminated referred to off-licence data so that the context of such references was clear. The Panel noted that there was a difference between interacting with a health professional as a prescriber and interacting with him/her as a consultant. Interactions with a health professional in his/her capacity other than as a prescriber, eg speaker training, might be considered non-promotional. In such circumstances, and where directly relevant, the provision of relevant unlicensed data to the health professional might not be contrary to the Code which prohibited the promotion of unlicensed data or data that was inconsistent with the terms of a product's marketing authorisation. The provision of such data to individuals who were training to be speakers should comply with the Code.

In relation to the meeting in question the Panel noted that no monies were paid to delegates who were not also presenting. The Panel noted that the contract for UK delegates was headed 'Support for individual attendance at an event' and did not refer to a training event; it appeared, in the Panel's view, akin to a contract for sponsorship to attend a clinical meeting as a delegate. The Panel noted its comments above about the impression given by the title of the meeting.

The Panel noted that the health professionals who attended and who were existing members of the faculty and who, unless presenting at the meeting in question, were invited for the second day and had the option to also attend on day one; new members to the faculty were invited to attend both days.

The Panel queried whether the purpose of the meeting was sufficiently clear at the outset to all invitees, particularly new faculty members. In the Panel's view the emails were not sufficiently clear that the primary purpose of the meeting in question was to train speakers and that the clinical data was presented for that purpose, rather the emails implied that it was an invitation to attend a meeting about oncology therapy and idelalisib, part of which would include presentation skills training. Whilst some details about the presentation skills sessions were given in the detailed agenda, the agenda still appeared primarily to describe a clinical meeting and did not negate the otherwise misleading impression about the primary purpose of the meeting given by the invitation emails. The reference to the faculty programme in the invitation and agenda implied that there was an ongoing clinical programme.

The Panel noted Gilead's submission about the selection criteria. The Panel did not know when the UK delegates had first been contacted to attend the meeting but noted that an email dated 26 July 2017 from the European company asked affiliates to nominate local health professionals and implied that the primary purpose of the meeting in question was to enable delegates to acquire in-depth clinical knowledge, including about idelalisib. Although the email dated 26 July referred to training and speakers, the Panel considered that overall this was not given sufficient prominence; training was presented as just one of several benefits of the meeting. In addition the rationale for selection subsequently given by the UK affiliate to the European company did not refer to the potential delegates' suitability as speakers and the company's intention to engage them as such. Although the UK company subsequently confirmed to the European company that 'the plan is to engage the HCP', there was no evidence before the Panel that UK health professionals had been so informed.

The Panel noted Gilead's submission that the purpose of the meeting and expectations of delegates after the meeting were clearly communicated at the meeting itself, this was too late. The Panel considered that the failure to make the intended purpose of the meeting sufficiently clear at the outset meant that high standards had not been maintained. A breach of the Code was ruled. The Panel noted its comments above about the impression given by the arrangements and considered that invitees would, on the balance of probabilities, consider that they were being invited to a promotional meeting and in this regard the Panel did not consider that the meeting was a disguised promotional activity. No breach of the Code was ruled.

The Panel noted the complainant's allegation that the meeting was not balanced education and that promotional techniques were used throughout. The complainant stated that examples were chosen of idelalisib in a positive light and competitors in a negative light and had referred, in particular, to a statistics presentation. The Panel noted the complainant bore the burden of proof and had not explained why the particular worked examples were disparaging; he/she had not provided sufficient detail to establish why the presentation in question was disparaging or unbalanced. No breach of the Code was ruled.

The Panel noted that the complainant alleged that the co-chair was biased and had, in particular, referred to the increased risk of infection associated with a competitor. Gilead submitted that the latter comment was a statement of fact and referred to the infections listed as common in the relevant SPC. It was not clear precisely what had been said by the co-chair although it was clear that he/she had commented on the subject matter of the complaint. The Panel also noted Gilead's submission that the comments were made in response to an unsolicited question. Noting that the complainant bore the burden of proof, and Section 4.8 of the competitor SPC, the Panel considered that it had not been established that comments by the co-chair about the competitor were unbalanced. No breach of the Code was ruled on this point.

In relation to an allegation that the co-chair was biased as he/she questioned the validity of data on another competitor, the Panel noted Gilead's submission that it had no recollection of the co-chair making such a statement and that this was reflected in the meeting summary. The Panel noted that the responses in the meeting summary did not appear to question the validity of the competitor data as alleged. The complainant bore the burden of proof. The Panel considered that it had not been established that the validity of the data had been questioned as alleged. No breach of the Code was ruled.

The Panel noted the allegation that the Gilead co-chair deliberately asked questions of speakers so that positive idelalisib data would be discussed, including off-label data. The Panel considered that given the product and therapy area, speakers might be asked questions about unlicensed data and it was not unreasonable to train them to address such questions so long as, overall, the activity otherwise complied with the Code. The Panel noted that the complainant bore the burden of proof. The Panel noted its concerns above but, on balance, considered that there was insufficient evidence before it and no breach was ruled.

The Panel noted the allegation that idelalisib was being positioned as a preventative treatment for

Richter's transformation in CLL and that there was no data to support these claims. The Panel noted idelalisib's licensed indication as part of the treatment of certain adult patients with CLL. The Panel noted its general comments above about the provision of data about the unlicensed use of a product as part of a formal speaker training event.

The Panel noted Gilead's submission that a presentation entitled 'Prevention of Richter's transformation' was provided to train participants on the clinical unmet need in patients with CLL who progress with Richter's transformation. Gilead also stated that the session was delivered to train participants to respond appropriately if asked about this topic when delivering presentations on idelalisib. The Panel considered that given the therapy area, in principle, it was not unreasonable, within the context of *bona fide* speaker training, to train participants to answer unsolicited questions about the off-licence use of a product.

The Panel noted that the presentation in question 'Prevention of Richter's transformation' was delivered on the afternoon of the final day. The summary slide described Richter's transformation as an unmet clinical need in CLL patients; the immediate preceding slide implied that Zydelig might satisfy that unmet clinical need. The Panel considered that other presentations also discussed idelalisib and Richter's transformation in positive terms. The Panel considered that the overall narrative of the presentations was such that they highlighted features of idelalisib, including its unique mechanism of action, in relation to the prevention of RT which was described in the final presentation as an unmet clinical need. The Panel considered that the presentations, together with the description of such comparative data as 'potentially practice changing' by a speaker who Gilead described as a globally respected expert and principal investigator was such that, on balance, the company positioned Zydelig as a preventative treatment for Richter's Transformation as alleged. A breach of the Code was ruled.

In relation to the allegation that Gilead accepted and verbalised the hypotheses about idelalisib being an 'immuno-oncology compound which supresses the high risk clones' without data to support such claims, the Panel noted Gilead's submission that it had no recollection or record of this being stated at the meeting. The Panel noted that the comment, or one closely similar, did not appear in the summary of Q&A. The Panel therefore considered that the complainant, who bore the burden of proof, had not established that the statement had been made and, on this basis, no breach of the Code was ruled.

In relation to the complainant's allegation about an imbalance of delegates from Italy, the Panel noted Gilead's explanation, including that the product was launched in Italy a few months before the safety signal emerged in March 2016 and Italian clinicians had little experience in managing adverse events at that time. The Panel did not consider that the proportion of Italian participants alone rendered the meeting inappropriate as a training event. No breach was ruled on this narrow point.

An anonymous, non-contactable health professional complained about a Gilead Oncology Faculty Meeting held in Frankfurt in March 2018 which was described by Gilead as a speaker training meeting for Zydelig (idelalisib). Zydelig was used in certain adult patients with either chronic lymphocytic leukaemia (CLL) or follicular lymphoma (FL).

COMPLAINT

The complainant explained that he/she had been invited to attend a non-promotional Gilead Oncology Faculty Meeting which was organised and fully funded by Gilead.

The complainant stated that his/her main concern was that the meeting constituted disguised promotion. Despite being told on numerous occasions, verbally and on slides during the meeting, by the organisers that the meeting was non-promotional, he/she considered that Zydelig was promoted throughout the two days.

The complainant stated that it was only after arriving that he/she found out that the premise of the meeting was to train speakers on Zydelig and for them then to go out and speak about the medicine. Before the meeting, it was not made entirely clear that this would be the expectation following the meeting.

The complainant submitted that the content was not balanced medical education. Just because slides did not contain brand names/logos or overt promotional claims but did discuss safety/side effects did not make the meeting non-promotional. The complainant stated that he/she would expect that side effects were discussed during any interaction with a company representative. That was responsible promotion.

More subtle promotional tactics were used throughout the meeting eg Zydelig was shown in a positive light and competitors in a negative light. The meeting revolved around Zydelig. Even in a statistics lecture, the examples were chosen to cast doubt on either competitor data, or data which could be perceived as negative for Zydelig. The complainant alleged that this disparaged one competitor medicine in particular and was clearly promotional in tone and content.

The complainant alleged that the meeting co-chair from Gilead was overtly biased. At a non-promotional meeting, it would be expected that a company co-chair, would only move the meeting along in terms of timing/logistics and act as master of ceremonies. At the meeting in question, the co-chair actively took part in discussions, discussed data and actively directed the meeting in a way that the complainant would have expected at a promotional meeting. The co-chair brought up positive aspects of Zydelig and disparaged competitors with statements such as '[one medicine] has a lot of problems with infections' and questioned the validity of data on another which had recently been published in the

New England Journal of Medicine and which the complainant considered was so much better than the Zydelig data in CLL.

Furthermore, the Gilead co-chair deliberately questioned the speakers so that positive Zydelig data would be discussed, even off-label data. The co-chair proactively asked questions of speakers on favourable off-label Zydelig data eg a question on the RIALTO study – a frontline off-label combination of Zydelig. This was deliberately done to build a favourable image for Zydelig. The co-chair tried to get one of the speakers to state that after only 2.5 months of treatment with Zydelig there were long responses. The co-chair succeeded and a speaker spoke favourably about this study and potential long-term effects of Zydelig. The complainant noted that this discussion was based on off-label data, from a study which was stopped due to safety concerns, where a number of patients died due to Zydelig-related infections. This data was proactively referred to again on day two by another Gilead employee.

The complainant stated that on day two he/she was appalled to hear Zydelig positioned as a preventative treatment for Richter's transformation (RT) in CLL. There was no data to support those claims; it was all hypothesis and postulation. Tables showing different rates of RT with the different novel agents were shown and even the speaker said a number of times that any observed difference should be 'taken with a pinch of salt' due to differences between the studies and a number of other factors. The complainant submitted that cross-trial comparisons were risky and confounded.

Gilead appeared to accept and verbalize the hypotheses that Zydelig was an 'immuno- oncology compound which suppressed the high-risk clones as fact, without any data to support the claims. A table used to highlight a lower rate of RT with Zydelig used data from off-label studies – this slide was freely available for delegates to download afterwards from the Gilead Oncology Faculty Portal. The complainant alleged that there was off-label data throughout the portal (which consisted of hundreds of slides).

The complainant also noted the imbalance of attendees from certain countries – half were from Italy. The complainant queried whether they all went out and talked about Zydelig following the meeting, or even a substantial proportion of them. The complainant submitted that it appeared to be a reasonably efficient way for Gilead to have a large contingent held captive for two days while paid speakers promoted to them.

Overall, the complainant stated that a two day meeting discussing one product was wrongly classified as non-promotional; he/she objected strongly to the disguised promotion and constant disparaging of competitor molecules which were equally, or in most cases, more effective than Zydelig. The constant interference in the proceedings by an obviously biased Gilead employee, who proactively asked about off-label data, was unacceptable.

When writing to Gilead, the Authority asked it to respond to the requirements of Clauses 2, 3.2, 7.2, 7.3, 7.4, 8.1, 9.1, 11.1 and 12.1.

RESPONSE

Gilead explained that the meeting was organised by Gilead Sciences Europe Limited (GSEL), Gilead Science's headquarters for the Europe, Middle East and Australia (EMEA) region. GSEL was based in the UK.

Gilead did not consider that its arrangements for the meeting breached the Code. The meeting was an appropriate training meeting held to ensure that those health professionals whom GSEL intended to engage to speak on its behalf had a full and detailed understanding of the Zydelig data set. This meant that when they were engaged to present at Gilead-organised meetings they could present the data in a way that reflected the evidence for Zydelig in line with its marketing authorization.

Attendees were selected on clear and appropriate criteria and they were told about the nature and purpose of the meeting through the invitation process and again at the start of the meeting. The attendees were not paid for their attendance, unless they were specifically engaged to present during the meeting.

The meeting content consisted of appropriate and necessary education required to achieve the stated purpose. The content was accurate, balanced, fair, and could be substantiated. Any off-label information was clearly highlighted and only shared to ensure that participants fully understood the data set for Zydelig and could reflect the evidence for the medicine in line with its marketing authorization when engaged by Gilead. The attendees were trained on GSEL's requirements in relation to sharing any off-label data proactively, and how to appropriately handle any questions on off-label data.

Background to the meeting and licensed indications for Zydelig in Europe

The meeting was the Gilead Oncology Faculty meeting and was held to train the invited European health professionals on the latest clinical data and evidence related to Zydelig. The training was to prepare the delegates to speak about Zydelig on behalf of Gilead at company-organised meetings in countries within the region. GSEL had held a face-to-face Oncology Faculty training meeting once a year since 2015 (there were two held in 2015 when the Faculty was launched). A virtual meeting was also held in 2017.

Zydelig was indicated in Europe as follows:

> 'Zydelig is indicated in combination with an anti-CD20 monoclonal antibody (rituximab or ofatumumab) for the treatment of adult patients with chronic lymphocytic leukaemia (CLL):
> - who have received at least one prior therapy, or

- as first line treatment in the presence of 17p deletion or TP53 mutation in patients who are not eligible for any other therapies

Zydelig is indicated as monotherapy for the treatment of adult patients with follicular lymphoma (FL) that is refractory to two prior lines of treatment.'

On 10 March 2016, the European Commission (EC) was informed that an increased risk of death and a higher incidence of serious adverse events had been seen in Zydelig patients compared with the control groups in three Gilead sponsored clinical trials (NCT01980888, NCT01732913 and NCT01732926). The Pharmacovigilance Risk Assessment Committee (PRAC) subsequently assessed the risk/benefit of Zydelig in its licensed indications. The EC's final decision and assessment report resulted in the licensed indications as stated above.

The meeting provided the future speakers with accurate, balanced information about the safety and efficacy of Zydelig. The objective of the meeting was to ensure that they fully understood the data for Zydelig and its safety management to ensure they could present the data in a way that reflected the evidence for the medicine in line with its marketing authorization. Given the safety issues identified above, the complex safety profile of the medicine and the need for careful safety management of patients, the Faculty was a critical platform for ensuring patient safety.

Delegate selection and participation

GSEL maintained a register of trained speakers who could be engaged by Gilead country affiliates to speak about Zydelig - the Gilead Oncology Faculty ('the Faculty').

The meeting was held to train both new and existing members of the Faculty; it was structured as follows:

Day one was for new members to the Faculty and provided training, delivered by existing expert members of the Faculty, on the on-label Zydelig data. An agency delivered an interactive presentation skills training session about the importance of good presentation including preparation and presentation. Existing members of the Faculty who wanted to refresh their knowledge could opt in to day 1 if they wished.

Day two was for new and existing members of the Faculty and it provided training on new Zydelig on-label data (recent data from the preceding 12 months) and topics of relevance. Further interactive speaker skills training was provided.

The GSEL medical team worked with country affiliate medical teams to identify suitable potential new members to the Faculty. The potential new members invited to the meeting were selected based on their:

- ability to educate their peers about scientific information relating to Gilead's products and the diseases they treated;
- knowledge, expertise and skills to explain complex data and
- therapeutic experience required to respond appropriately to audience questions.

These criteria were communicated to delegates on day one of the meeting to provide further clarity on their role. In addition, the new Faculty members were selected on the basis that they:

- were already recognised as speakers or they wished to become speakers;
- expected to be engaged to speak at Gilead meetings;
- had a good professional standing within the haematology-oncology community;
- could speak engagingly in front of a larger group; and
- were likely to be available to take on additional speaker engagements.

As well as the new Faculty members, existing Faculty members were invited to the meeting provided they continued to meet the above criteria and provided the country affiliate teams continued to intend to engage them to speak on Gilead's behalf. Eight members of the Faculty were engaged to present at the meeting.

What were the participants expected to do after the meeting?

After the meeting delegates were expected to speak about the safety profile and efficacy of Zydelig, and its safety management at Gilead-organised events. The content for the meeting was focused on the topics that the delegates would be expected to present on in future events and to prepare them to appropriately answer questions from the audience. The meeting thus focused on Zydelig, with other approved agents mentioned where appropriate.

This expectation was highlighted in the invitations to the meeting and repeated on day one when the participants were briefed as to why they were selected and on Gilead's expectations and rules of engagement when they presented on Gilead's behalf.

How many attended the meeting and were they paid? Participant list and their country of practice.

GSEL provided a list of the 11 new and 11 existing Faculty members and the 8 external Faculty speakers who attended the meeting in addition to the 7 Gilead attendees. GSEL identified which days of the meeting they each attended and their countries of practice. There were 5 external participants from the UK - 3 Faculty speakers, 1 existing Faculty member and 1 new Faculty member. The meeting was facilitated by an external medical agency engaged by GSEL.

Faculty members who were engaged to present at the meeting were only paid for the time they spoke or participated as indicated on the agenda. The participants attending as new or existing Faculty members were not paid to attend the meeting but GSEL met their reasonable costs (or paid direct) for hospitality (travel, accommodation and subsistence) in accordance with GSEL's policy.

How many of the participants had presented for Gilead at other meetings?

All of the Faculty members engaged to present at the meeting had been engaged by Gilead and had delivered at least 59 presentations across the EMEA region since they became Faculty members. Gilead had engaged 4 of the other existing Faculty members attending the meeting to present on 14 occasions since they became Faculty members. The majority of these Faculty members first joined the Faculty in 2017.

Gilead maintained the Gilead Oncology Faculty so that it had a pool of speakers with an up-to-date knowledge of Zydelig who were able to speak on its behalf in a knowledgeable and compliant manner. Whether they were engaged to present could depend on many factors.

If a Faculty member had not been engaged to speak, this was a factor as to whether they were retained in the Faculty and invited to future training meetings, and this was monitored by the EMEA medical team. A lack of engagement would not necessarily mean they were removed from the Faculty and excluded from future training provided there was a continued intention to engage them (and there was an anticipated demand for meetings such that it was likely they would be engaged) and there was a good reason why future training to update their knowledge was considered necessary.

This was reviewed and discussed jointly by the EMEA and country medical teams. Given the detailed and technical product knowledge that speakers required, Gilead considered the Oncology Faculty meeting was an important training event for them, in particular for new or recently joined members.

How many Gilead staff attended, how were they selected and their roles?

Seven Gilead medical affairs staff from EMEA headquarters or from countries who nominated participants attended the meeting. No sales or marketing personnel attended. The selection of the medical team members was based on defined criteria.

A full list of the Gilead staff members who attended and their roles was provided.

Code considerations

With regard to the complainant's comments that the objective of the meeting (to train speakers on Zydelig) had not been made clear beforehand, GSEL explained that all participants, including those from UK, were informed in advance that the meeting was a training meeting as part of the Gilead Oncology Faculty programme. This was indicated on the email which invited the participants to register for the meeting and in the verbal discussion with the new participants inviting them to be members of the Gilead Oncology Faculty speakers programme.

The country teams had to speak to new Faculty members to explain to them the expectation that they would be asked to speak on behalf of Gilead at Gilead-organised events and to ensure that they were happy to be available to do this. The purpose of the meeting, and expectations after it, were again clearly communicated at the start and throughout the meeting, for example, in a presentation 'Your relationship with Gilead and participation in the Oncology Faculty' (copy provided). GSEL thus did not consider that the meeting was in breach of Clause 11.1 of the Code; it was reasonable to assume that all those attending were aware of the nature of the material they would receive and were happy to receive it. Gilead also denied a breach of Clause 12.1 as the meeting was a training meeting and not a promotional meeting and the purpose of the meeting was made clear to all attendees.

The content was driven by topics on Zydelig on which these speakers might speak proactively in future or be able to respond appropriately and compliantly to questions that audiences might ask. There was a focus on Zydelig, with other approved targeted agents also mentioned throughout the training where appropriate and relevant. There were substantial discussions on both days focused on adverse events and management of Zydelig; whole sessions were dedicated to on-label adverse event management and understanding the mechanisms of toxicity. On day one an hour was dedicated to the safety profile of Zydelig, adverse event management and the patient with questions and answers on these topics. In addition, there was 45 minutes given to three clinical cases in patients with CLL and FL, describing the adverse events and its management. On day two there was 35 minutes dedicated to the mechanism of action of Zydelig and its immune-mediated events.

Throughout the meeting, only 25 minutes were dedicated to the efficacy of Zydelig in the pivotal clinical trials. Indeed an hour was dedicated to the safety profile and safety management of Zydelig. The clinical cases presented provided a good balance between the efficacy and safety of Zydelig and how patients on Zydelig should be managed. Furthermore, on day two, the sessions on the mechanism of action provided the rationale for the efficacy as well as for the observed adverse effects with Zydelig.

On the topic of balance of the meeting, there were several instances where information on the mechanism of action and activity of competitors were discussed, as detailed below:

- the role of Bruton's tyrosine kinase (BTK) on the microenvironment and on the malignant B-cell as well as the implications of BTK inhibition
- the mechanism of action of the three targeted agents approved in CLL.

There was opportunity for exchange of information, the audience was invited to contribute to the session and to challenge or affirm the presented information. At the end of each data presentation there was time allocated for discussion, as follows:

- Zydelig safety profile: 25 minutes
- Adverse event management and the patient: 25 minutes
- Discussion: 10 minutes
- Masterclass: Analysing and critically appraising medical statistics: 1 hour
- Discussion: 15 minutes
- Zydelig mechanism of action: Immune-mediated activity and transformation: 20 minutes
- Discussion: 15 minutes
- Crosstalk: Genomic landscape of high-risk CLL and prevention of transformation
- Genomic architecture and clonal evolution in CLL: 25 minutes
- Prevention of Richter transformation: 25 minutes
- Joint discussion: 30 minutes
- Final questions and discussion: 10 minutes.

Overall, there were 90 minutes allocated to discussion between the attendees and the speakers to ensure the attendees were able to ask questions on any areas they did not fully understand. The feedback from participants did not indicate that any considered the meeting was inappropriate or not what they had expected, including the feedback provided by the new and existing UK Faculty members. Thus, Gilead did not consider that, in the context of a speaker training programme for Zydelig, the meeting was anything other than appropriate and the content was balanced and non-promotional. The company denied a breach of Clauses 7.2 or 12.1.

Gilead noted the complainant's comment that Zydelig was shown in a positive light, with doubt cast upon data perceived as negative for the medicine, and that competitors were disparaged and his/her reference to a statistics lecture. In response, Gilead stated that in line with the objective of the meeting identified above, the statistics lecture presented by an expert statistician was designed to provide the participants with the knowledge necessary to fully understand the statistics of medical studies, in particular as they related to key studies in this therapeutic area so that they could present clinical data accurately when engaged by Gilead to do so.

The presentation contained many case examples related to the topics discussed including those related to Zydelig and its competitors in the trials. These examples were provided as real-life case studies to statistical principles being discussed by the presenter. Multiplicity considerations were discussed with the goal of understanding the meanings of statistical significance, nominal significance and clinical meaningfulness. The statistical robustness of a competitor study or the fact that it achieved its primary endpoint was never questioned. With regard to the secondary endpoints, it was clarified by the presenter (as shown on the slides) that the improvement in overall survival was nominally significant and considered clinically meaningful by the authors. This information was accurate, balanced, was fair, and could be substantiated. Gilead disagreed with the complainant and thus did not consider that the lecture was promotional or that it disparaged other medicines. Gilead thus denied breaches of Clauses 7.2, 7.3, 7.4, 8.1, 12.1.

With regard to the complainant's criticism of the co-chair, Gilead explained that in addition to keeping the meeting running on time, the co-chair invited attendees to participate in the training and this could be welcomed especially when there were silences or natural pauses.

In relation to the complainant's allegation about the co-chair's remark about one competitor, Gilead stated that it was difficult to respond specifically as the company had no recollection of him/her making any statement about the competitor at the meeting and this was not included in the report of the meeting. In any event the co-chair did not intend to disparage other medicines and in relation to the statement on a second competitor, this was a statement of fact, the reference for which was provided.

The internal report of the meeting confirmed that the comment on the incidence of infections with a competitor was made in the context of an unsolicited question from one of the attendees about the use of Zydelig or the competitor in patients with liver disease or smoking-related lung disease. The pertinence of this question was founded on the risk of transaminitis and pneumonitis seen with Zydelig. One of the speakers responded and clarified that it was currently not clear whether smoking-related lung problems increased the risk of pneumonitis in patients receiving Zydelig, so in these patients any of the small-molecule therapies could be considered. The co-chair alluded to the topic of infections due to the risk of community-acquired pneumonia in patients with smoking habits, which could be aggravated by the increased risk of infections (including pulmonary) observed with Zydelig. To be fair and balanced, the co-chair mentioned that infections, including pneumonia, had also been observed with a competitor. In fact, infections with the competitor were mentioned in its summary of product characteristics (SPC) as a very common adverse drug reaction (≥ 1/10) and referred to in the section 'Special warnings and precautions for use'. Pneumonia, upper respiratory tract infection and sinusitis in particular were each mentioned as very common (≥ 1/10) drug reactions with the medicine. As could be attested by the SPC provided, this comment was accurate, balanced, fair, and could be substantiated.

Again, the co-chair did not intend to disparage other medicines, nor did he/she do so. The discussion was in response to a question, was balanced and reflected the most recent evidence available. Gilead denied breaches of Clauses 7.2, 7.3, 7.4, 8.1 and 12.1.

Gilead noted the complainant's comment that the co-chair asked questions that would result in the positive discussion of Zydelig, including discussions of off-label data, and appeared to deliberately support and build a favourable image of Zydelig.

Gilead considered that the discussions on the RIALTO study were in the context of an unsolicited question raised by one of the attendees on the availability of data about the maintenance of off-treatment response in patients who stopped Zydelig due to adverse events. An anecdotal clinical case

had been presented before this discussion. As there was no on-label information that could be shared about this topic, the co-chair invited one of the speakers to comment on one of his/her studies where a similar situation occurred: patients were treated with Zydelig for a median of 2.5 months and stopped treatment due to a safety signal. Published data on this study demonstrated that the patients treated with Zydelig for a median of 2.5 months had not progressed quickly, as seen in the progression free survival K-M curves (Pettitt, *et al* 2017). Gilead noted that the treatment in this study was stopped in the context of a safety signal observed in the previously mentioned three clinical trials sponsored by Gilead in 2016. Indeed, the treatment in the RIALTO study was not stopped due to data emerging from that particular trial, as could be implied from the complaint. The intent was solely to respond to an unsolicited question and to clarify the outcomes after stopping Zydelig treatment in this study and not to induce the prescription of Zydelig as per the inclusion criteria of RIALTO.

As per the meeting report, Gilead's answers in response to individual enquiries from members of the audience, were accurate, not misleading and it was clearly mentioned it was off-label and the response was restricted to that necessary to answer the question and ensure the attendee had a clear understanding of the relevant data for Zydelig. Understanding and recognising off-label data was important so that those engaged to speak on Gilead's behalf could do so compliantly in line with the instructions it gave on handling off-label questions.

Gilead stated that it provided clear guidance to those it engaged to speak about its products and in particular provided guidance on how to handle off-label questions that came for the audience. This guidance was presented to attendees on day one.

Gilead denied breaches of Clauses 3.2, 7.2, 7.3, 7.4, 9.1 and 12.1.

In response to the complainant's allegation that Zydelig was positioned as preventative treatment for Richter's transformation (RT) in CLL, Gilead explained that on day two a presentation 'Prevention of Richter transformation' from a globally respected expert haematologist informed participants about the unmet clinical need in CLL patients who progressed with Richter's transformation, an aggressive lymphoma transformation of CLL which occurred in approximately 3-10% of relapsed/refractory CLL patients. These patients had very limited treatment options with survival lasting only for a few months after conventional treatment.

Details of the presentation were provided.

The session trained participants to respond appropriately if asked about this topic when delivering Zydelig presentations. This was a topic of importance in the community (Khan *et al* 2018) and questions on it could be anticipated when members of the faculty presented in their subsequent speaker engagements.

As with all difficult to treat conditions, exploration of different strategies was rightly required in clinical trials. The speaker made it absolutely clear what the hypotheses were and what remained to be tested in prospective clinical trials. Gilead agreed with the complainant that different rates of Richter transformation had been noted with different novel agents so far and that indirect comparisons were always confounded as trial populations were different.

The speaker emphasised at the start of his/her presentation that he/she considered the best way to prevent Richter transformation was to treat CLL effectively, which considered all available therapies including conventional chemotherapy and novel agents. In this session, Zydelig was discussed for the treatment of CLL patients with high-risk disease, which included patients at risk of progression to Richter's transformation. Currently there were no biomarkers that could predict which patients would progress to Richter's transformation and when. These patients were treated, as any other CLL patient, with the treatments that were currently available, including Zydelig. The treatment of patients with CLL with high-risk was within the indication of Zydelig in CLL patients. Zydelig was not discussed for the treatment of Richter's transformation. Gilead did not 'position' Zydelig as preventive treatment to Richter transformation or as treatment for this condition and this session was provided in order that participants could address anticipated reactive questions on this topic in an informed manner in line with the guidance given on handling questions relating to off-label data. Gilead noted the complainant's objection to the inclusion of off-label data, but stated that this was considered necessary to ensure a complete and balanced position was provided to the participants, especially in relation to matters of safety. Gilead denied breaches of Clauses 3.2, 7.2, 7.3, 7.4, 8.1, 9.1 and 12.1.

With regard to the complainant's allegation that the hypothesis that Zydelig was an immuno-oncology compound which suppressed the high-risk clones, was presented as fact with no supporting data, Gilead stated that it had no recollection or record of this being stated at the meeting. Gilead submitted that the reference to a table being shown was likely to be a reference to a slide shown by the expert haematologist and, in that regard, its response on that slide was as stated above. Gilead denied breaches of Clauses 3.2, 7.2, 7.3, 7.4, 9.1, 11.1 and 12.1.

With regard to the number of Italian attendees, Gilead explained that in line with Italian requirements, the arrangements for the meeting, including the agenda and details of the Italian health professionals attending, were submitted for review by the Italian Medicines Agency (AIFA) and approved before the meeting took place.

All attendees were chosen based on the selection criteria referred to above. Having applied these criteria, the Italian Faculty members (new and existing) were invited to register for the meeting and the number registering to attend from Italy was higher than from any other countries. All met the criteria, and all wanted to maintain up-to-date knowledge so that they could speak accurately when presenting to other health professionals. The Gilead Oncology Faculty was a pool of trained speakers

who might be engaged by any country in the region to present on the topics covered by the Faculty, not just in their country of practice.

Zydelig was launched in Italy a few months before the safety signal emerged in March 2016 and when the Italian clinicians had little experience in managing the adverse events with Zydelig. Since then, the Gilead Oncology Faculty had been an important platform to train speakers who had then educated Italian clinicians on the appropriate use of Zydelig. Gilead considered that this initiative had positively contributed to the appropriate management of Zydelig and ultimately to the safety of patients.

Accordingly, Gilead considered that the arrangements for this training meeting were appropriate, including the appropriateness of each of those attending, and specifically each of the Italian attendees. All participants invited met the strict criteria set. The company did not consider that it had breached any clause of the Code in relation to this aspect of the complaint and in particular considered that the requirements of Clauses 11.1 and 12.1 had been met.

In conclusion, Gilead considered that GSEL's arrangements for the meeting met all the requirements of the Code. The event was an appropriate training meeting held to ensure health professionals GSEL intended to engage to speak on its behalf had a full and detailed understanding of the data set so that when they presented at Gilead organized meetings they could present the data in a way that reflected the evidence for Zydelig in line with its marketing authorization. Attendees were selected on clear and appropriate criteria and were told about the nature and purpose for the meeting through the invitation process. The attendees were not paid to attend unless they were engaged to present at the meeting.

In the light of its detailed response on all issues raised by the complainant, GSEL considered that it had adopted high standards in its arrangements for the meeting and did not accept that the arrangements were such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. The company thus denied breaches of Clauses 2 and 9.1.

FURTHER INFORMATION FROM GILEAD

Gilead submitted that two UK delegates were invited to the meeting and each was invited directly by email. One of the delegates was nominated to be invited as a new faculty member by the UK head office based on certain criteria in particular that the UK team planned to engage him/her in Gilead sponsored meetings in 2018. The other UK delegate was an existing faculty member and so invited to update the training he/she first received in 2017. The UK team nominated him/her to attend based on a continued intention to engage him/her to speak on Gilead's behalf.

GSEL provided written and verbal guidance for staff throughout the preparations for the meeting. Information to the countries on the meeting was provided in the form of emails to the EMEA region and country specific e-mails, including guidance on speaker selection and invitation and monthly update calls organised by GSEL with the countries to provide updates, guidance, and request feedback from the countries (the Oncology Network Meetings). At the meetings the guidance in relation to the nomination and invitation process was given verbally.

- Reminder that the Gilead Oncology Faculty was the oncology speakers' programme and that the meeting was an opportunity to train new Faculty members or retrain existing members. Request for teams to nominate new Faculty members, who should attend on both days of the meeting. The country teams should contact the new Faculty members to explain the programme and assess their interest and availability for subsequent speaker engagements, and the agency would follow up with the clinicians with a formal invitation. Request for the team to identify existing Faculty members who they would like to invite to attend Day 2 only for update training. An option was given for the teams to either contact the existing members first followed by a written invitation by the agency, or the agency would contact the Faculty directly once nomination was received from the country team.

- Any nomination of new Faculty members should be local health professionals that the team already recognised as speakers and that they intended to engage in local/regional and the selection criteria (identified above) were set out.

Gilead provided copies of the UK attendees' agreements and gave details of when each had been engaged to speak on behalf of the company.

Gilead considered that the meeting was a non-promotional training meeting, but the presentations that trained faculty members subsequently gave could be promotional or non-promotional, depending on the content and context.

The statistician who also presented at the meeting and had not otherwise been engaged to speak in the last 12 months.

The Gilead UK Oncology team organised two types of meetings for health professionals – (i) regional meetings for which Gilead engaged as speakers faculty members who were leading experts; and (ii) localised meetings for which Gilead typically engaged newer faculty members. Shortly after the meeting was held, Gilead changed its priorities and organisation resulting in the field team in the region where two delegates were based being reduced to one medical scientist. Local meetings were consequently no longer being organized and the focus had been on regional meetings only. These changes were not foreseen when the meeting in question was held.

Gilead submitted that the faculty members who had not been engaged to speak did not still have access to the portal. In fact, no members of the faculty currently had access to the portal; Gilead was providing the necessary documents from the portal

to speakers as and when they were engaged to present on behalf of the company.

Gilead stated that the attendees were trained during the meeting on GSEL's requirements in relation to sharing any off-label data, and how to appropriately handle any unsolicited questions on off-label data that might arise when they were engaged to speak.

Guidance on handling unsolicited off-label questions from the audience in Gilead sponsored events was presented by Gilead on day one of the meeting under the topic 'Speaker engagements'. The presentation specifically mentioned that responses to unsolicited off-label questions needed to be objective, balanced, scientifically rigorous, and within the scope of the question. Once a concise answer limited to the scope of the question was provided, the speaker should immediately return to the approved presentation.

The speakers were also reminded that if they were informed of any off-label use of Gilead products, they were required to report that safety information to Gilead within 24 hours of becoming aware of the event.

PANEL RULING

The Panel noted that the meeting in question took place in Germany and was organised by the UK based affiliate, Gilead Sciences Europe. The Panel noted that the meeting had to comply, *inter alia*, with the UK Code. The Panel noted that the UK company, Gilead Sciences Limited, was responsible for the acts and omissions of its UK based European affiliate that came within the scope of the Code. The Panel noted that Gilead Sciences Europe had responded to the complaint.

The Panel noted Gilead's explanation that the Gilead Oncology Faculty was a register of trained speakers. The Panel noted the title of the meeting, Gilead Oncology Faculty meeting, and queried whether it fairly reflected the stated purpose of the meeting. In the Panel's view such faculties were often used to describe company convened meetings of key opinion leaders and such like. The impression given by the title of the meeting was important.

The Panel noted Gilead's submission that the meeting in question was an appropriate training meeting to ensure that health professionals whom the company intended to engage to speak on its behalf had a detailed understanding of the clinical dataset. The Panel considered that training speakers was an important and legitimate activity; the overall arrangements and content had to comply with the Code. When determining whether the content was appropriate the Panel considered that the overall arrangements, the therapy area and the professional status of the delegates were relevant. In the Panel's view it should be made clear to delegates at the outset and prior to their attendance that the meeting in question was a speaker training event and that they would be engaged as speakers thereafter. The Panel noted that speaker contracts were covered by Clause 23 which applied to contracts with consultants. The Panel considered that in principle it was good practice when training speakers to fulfil future speaker engagements to ensure that a written agreement covered the training activity to ensure that the arrangements including the nature of the meeting, the context in which data was presented and the parties' responsibilities and relationship were clear. Such written agreements were particularly important if the material disseminated referred to off-licence data so that the context of such references was clear. The Panel noted that there was a difference between interacting with a health professional as a prescriber and interacting with a health professional as a consultant. The Panel noted that if a company was interacting with a health professional in his/her capacity other than as a prescriber, such as training a health professional to speak on behalf of a company, such interaction might be considered non-promotional. In such circumstances, and where directly relevant, the provision of relevant unlicensed data to the health professional as part of such interaction might not be contrary to the provisions of Clause 3 which prohibited the promotion of unlicensed data or data that was inconsistent with the terms of a product's marketing authorization. The provision of such data to individuals who were training to be speakers should comply with the Code.

In relation to the meeting in question the Panel noted that no monies were paid to delegates who were not also presenting at that meeting. The Panel noted that the contract for UK delegates was headed 'Support for individual attendance at an event' and covered the quantification and disclosure of financial support to attend the meeting and its subsequent publication as a transfer of value. The contract did not refer directly or indirectly to a training event and appeared, in the Panel's view, akin to a contract for sponsorship to attend a clinical meeting as a delegate. The Panel noted its comments above about the impression given by the title of the meeting.

The Panel noted that attendees comprised health professionals who were existing members of the Faculty and who, unless presenting at the meeting in question, were invited for the second day, and new members who were invited to attend both days. The first day of the meeting was also open on an optional basis to existing members of the Faculty. The Panel did not have copies of the training materials on presentation skills.

The Panel queried whether the purpose of the meeting was sufficiently clear at the outset to all who were invited to attend, particularly as new faculty members. The Panel noted the invitation emails to the two UK participants dated 3 January (a returning faculty member) and 6 February 2018 (a new faculty member). The subject heading read 'Register for the meeting: Gilead Oncology Faculty Meeting, Frankfurt, 19-20 March 2018' and the first line of the email thanked the recipient for their interest in participating in the Gilead Oncology Faculty meeting (6 February) and their ongoing participation (3 January). The meeting was described as an interactive meeting which would 'provide training on idelalisib treatment and patient management, analysing medical statistics and practical presentation skills.' The opportunity for discussion with international

experts was referred to. The two day agenda was summarised in the body of the email; each day's summarised agenda referred to presentation skills training at the very end of a detailed list of clinical and statistical presentations. In the Panel's view the emails were not sufficiently clear that the primary purpose of the meeting in question was to train recipients of the emails as speakers and that the clinical data was presented for that purpose, rather they gave the impression that it was an invitation to attend a meeting about oncology therapy and idelalisib, part of which would include presentation skills training. In the Panel's experience it was not necessarily unusual for a clinical programme to include soft skills training such as presentation skills. The detailed agenda was attached to the email; day 1 had a 1.5 hour session on presentation preparation and a 10 minute session on speaker engagements; day 2 included 2 hours of presentation delivery/chairing skills. Whilst some details about the presentation skills sessions were given in the detailed agenda, the agenda still appeared primarily to describe a clinical meeting and did not negate the otherwise misleading impression about the primary purpose of the meeting given by the invitation emails. The reference to the faculty programme in the invitation and agenda implied that there was an ongoing clinical programme.

The Panel noted Gilead's submission about the selection criteria. The Panel did not know when the UK delegates had first been contacted to attend the meeting but noted that the email dated 26 July 2017 from the European company to local affiliates including the UK asked affiliates to nominate local health professionals. In the Panel's view that email implied that the primary purpose of the meeting in question was to enable delegates to acquire in-depth clinical knowledge, including about idelalisib. The list of 6 benefits of faculty membership, which one might reasonably assume that affiliates would highlight to potential invitees, included access to the faculty online portal which included a full idelalisib slide deck, case studies, the ability to create or download presentations, watch webcast presentations and symposia footage and the ability to submit questions. The final benefit referred to the opportunity to be invited to participate as a speaker at Gilead supported non-promotional events. In the Panel's view, the list of 6 benefits was inconsistent with Gilead's submission that the data at the meeting in question was presented in preparation for those invited to be engaged as speakers. The list of benefits made it clear that the portal material could be used for personal benefit unrelated to speaking at Gilead meetings. The email also referred to the opportunity to network and share clinical experience. The Panel acknowledged that the email dated 26 July did refer to training and speakers but considered that overall this was not given sufficient prominence; training was presented as just one of several benefits of the meeting. The Panel considered that it was supported in this view by the rationale for selection subsequently given by the UK affiliate in its email dated 1 December 2017 to the European company which nominated 12 new and 8 current members to attend the meeting in question and stated 'HCP with a special interest in FL/CLL who have engaged Gilead for educational support; HCP looking to extend their clinical knowledge and experience with targeted therapies'; suitability as a speaker and intention to engage them was not mentioned. The European company then asked the UK affiliate to approach the new members personally to explain the programme and what to expect and asked the UK affiliate to confirm that it planned to engage these new members as speakers in 2018. The UK company subsequently confirmed that 'the plan is to engage the HCP'. There was no evidence before the Panel that UK health professionals had been so informed. The Panel accepted that subsequent email correspondence from Gilead Sciences Europe to affiliates dated 29 November 2017 requesting case study nominations did refer to attendees as local speakers the affiliates were working with or were planning to work with.

The Panel noted the complainant's allegation that he/she had been invited to attend a non-promotional meeting and that before the meeting it was not made entirely clear that the premise of the meeting was to train speakers, and the content of the meeting was disguised promotion. The Panel considered that the primary purpose of the meeting should have been made abundantly clear at the outset when nominated individuals were contacted. Given the equivocal instructions to affiliates on this point as set out above in the email dated 26 July 2017, subsequent communications between the European affiliate and UK affiliate and its concerns about the invitation to UK delegates, the Panel did not understand how Gilead could be confident that all participants and, in particular, UK participants who had not previously attended a faculty meeting were clear from the outset that the meeting in question was a speaker training meeting. The Panel noted the complainant's comments on this point. The Panel considered, given its comments above, that on the balance of probabilities Gilead had not been unequivocally clear about the primary purpose of the meeting such that on arrival at the meeting an attendee who had not previously attended such meetings might consider that its stated true purpose, a training event, had, on the balance of probabilities, been disguised.

The Panel noted Gilead's submission that the purpose of the meeting and expectations of delegates after the meeting were clearly communicated at the start of the opening address and regularly during it but considered that this was too late, particularly for those who were new to the faculty and did not negate the failure to make the purpose clear to delegates prior to their arrival. The Panel considered that the failure to make the intended purpose of the meeting sufficiently clear at the outset meant that high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel noted its comments above about the impression given by the arrangements and considered that invitees would on the balance of probabilities consider that they were being invited to a promotional meeting and in this regard the Panel did not consider that the meeting was a disguised promotional activity and thus ruled no breach of Clause 12.1.

The Panel noted the complainant's allegation that the meeting was not balanced medical education and that subtle promotional techniques were used throughout the meeting. The complainant stated that examples were chosen of idelalisib in a positive light and competitors in a negative light and referred to the statistics presentation stating that examples were chosen to cast doubt on competitor data or data that could be perceived as negative for idelalisib, and that this was disparaging to one competitor in particular. The Panel noted that the statistics presentation entitled 'Analysing and critically appraising medical statistics' gave detailed explanations of statistical terms including several worked examples. A slide headed 'MURANO study ASH 2017' concluded that certain findings were exploratory only and could not be used as the basis for confirmatory claims. The Panel noted Gilead's submission that the statistical robustness of the study and that it achieved its primary endpoint were not put in question. The Panel noted the complainant bore the burden of proof and had not explained why the particular examples were disparaging. The Panel noted Gilead's submission that the presentation in question contained many examples including, *inter alia*, Zydelig and competitor trials. It was not always clear from the slides provided exactly what was discussed during the presentation of the slides in question. The Panel noted that the complainant bore the burden of proof. The Panel considered that the complainant had not provided sufficient detail to establish why the presentation in question was disparaging or an unbalanced comparison in this regard. No breach of Clauses 2, 7.2, 7.3 and 8.1 was ruled on this point.

The Panel noted that the complainant alleged that the co-chair was biased, examples referred to disparagement of competitor medicines. In relation to one particular competitor and infections, Gilead submitted that this was a statement of fact and referred to the infections listed as common in Section 4.8 of the relevant SPC. This listed four infections as very common, two as common and one as uncommon. The Panel noted that the summary Q&A for the meeting showed that in response to a question about the increased risk of transaminitis and pneumonitis in patients receiving idelalisib and management of certain patients a summarised answer read 'pulmonary infections have also been reported with other small molecule therapies, particularly [the competitor]'. The speaker was not identified in the summary but Gilead confirmed it was the co-chair who stated that infections including pneumonia had also been observed with the competitor. Gilead did not use the term 'particularly [the competitor]' in its response to this complaint. It was not clear precisely what had been said by the co-chair although it was clear that he/she had commented on the subject matter of the complaint. The Panel also noted Gilead's submission that the comments were made in response to an unsolicited question. Noting that the complainant bore the burden of proof, and Section 4.8 of the competitor SPC, the Panel considered that it had not been established that comments by the co-chair about the competitor were unbalanced. No breach of Clauses 7.2 and 7.3 was ruled on this point.

In relation to an allegation that the co-chair was biased as he/she questioned the validity of data on another competitor, the Panel noted Gilead's submission that it had no recollection of the co-chair making such a statement at the meeting and that this was reflected in the meeting summary. The Panel noted that the meeting summary did refer to discussion of the competitor data in response to questions, the identity of the speaker was not always clear but on the limited information before the Panel the responses in the meeting summary did not appear to question the validity of the competitor data as alleged. The complainant bore the burden of proof. The complainant had not identified the statements in question. The Panel considered that it had not been established that the validity of the data had been questioned as alleged. No breach of Clauses 7.2 and 7.4 was ruled.

The Panel noted the allegation that the Gilead co-chair deliberately asked questions of speakers so that positive idelalisib data would be discussed, including off-label data, and referred to a question to a speaker about the RIALTO study. The Panel noted Gilead's submission that the co-chair raised a question of a speaker to respond to an unsolicited question about the maintenance of off-label treatment response in patients who stopped idelalisib due to adverse events as a similar situation had occurred in that speaker's study and in a relevant anecdotal clinical case that had been presented by a different speaker prior to the discussion in question. The RIALTO study was subsequently referred to by the speaker in his/her response. The Panel had no detail about the case study but queried whether the question was, therefore, wholly unsolicited given the prior discussion and whether the company's response could truly take the benefit of the exemption to the definition of promotion in Clause 1.2, as implied by Gilead. The Panel noted that, contrary to the complainant's comments about the cessation of the study, Gilead submitted that it was stopped in the context of a safety signal observed in 3 different trials sponsored by Gilead. The Panel noted that both parties agreed that off-licence data was discussed. The Panel considered that it was not necessarily unacceptable to train speakers to respond to questions about off-licence data; whether it was acceptable would depend on a number of factors. The Panel noted its comments above in this regard. The Panel considered that given the product and therapy area, CLL and FL, speakers might be asked questions about unlicensed data and it was not unreasonable to train them to address such questions so long as, overall, the activity otherwise complied with the Code. The Panel noted that the complainant bore the burden of proof. The Panel noted its concerns above but, on balance, considered that there was insufficient evidence before it to determine whether Gilead had breached the Code on this matter. No breach of Clause 3.2 was ruled.

The Panel noted the allegation that idelalisib was being positioned as a preventative treatment for Richter's transformation in CLL and that there was no data to support these claims. The Panel noted

idelalisib's licensed indication in combination with rituximab or ofatumumab for the treatment of certain adult patients with CLL. The Panel noted its general comments above about the provision of data about the unlicensed use of a product as part of a formal speaker training event.

The Panel noted Gilead's submission that a presentation entitled 'Prevention of Richter's transformation' was provided to train participants on the clinical unmet need in patients with CLL who progress with Richter's transformation. Gilead also stated that the session was delivered to train participants to respond appropriately if asked about this topic when delivering presentations on idelalisib. The Panel considered that given the therapy area, in principle, it was not unreasonable, within the context of *bona fide* speaker training, to train participants to answer unsolicited questions about the off-licence use of a product. Context would be very important; it should be made clear that the provision of such data by a speaker during a promotional presentation should only be reactive and in response to an unsolicited question. That the speakers' response to an unsolicited question about the unlicensed use of a product should do no more that answer the question (and/or refer the question to medical information for a response) should be an integral part of any company's speakers' training presentation.

The Panel noted that the presentation in question 'Prevention of Richter's transformation' was delivered on the afternoon of the final day. The presentation described Richter's transformation and innovative trial designs to avoid clonal evolution in high risk CLL patients. Slides gave a clinical trial data overview and the incidence of Richter's transformation in certain patients treated with a competitor (six studies: 3-16%) and then idelalisib (nine studies: 2 - 2.4%). The Panel noted the summary slide described Richter's transformation as an unmet clinical need in CLL patients, referred to clonal evolution and stated that an understanding of the mutational landscape and pathways driving Richter's transformation may help define strategies to prevent transformation. The slide immediately preceding that summary was headed 'Idelalisib may prevent clonal evolution of high-risk CLL clones potentially resulting in the low rate of Richter transformation' which, in the Panel's view, implied that idelalisib might satisfy the unmet clinical need in Richter transformation referred to on the summary slide. The Panel noted the complainant's comment that the speaker said a number of times that any observed differences should be taken with a pinch of salt due to differences between the studies and a number of other factors. The Panel noted Gilead's submission about caveats made by the speaker during the presentation in relation to comparison of such data. The Panel noted that such caveats did not appear on the slides in question and considered that if such caveats were necessary for Code compliance the slides should be capable of standing alone in that regard. The Panel noted Gilead's submission that indirect comparisons with different novel agents were always confounded as the trial populations were different. The Panel had no way of knowing precisely what was said by the speaker. The summary of Q&A provided helpful guidance; a speaker, having noted the relatively low rates of RT with idelalisib, favourably compared idelalisib with its competitors and speculated on the effect that different modes of action might have. The presenter stated 'I consider the data highlighting differences in RT rates between different targeted therapies potentially practice changing in terms of how I use idelalisib in **CLL'** (emphasis added). The Panel noted that whilst both parties agreed that the speaker had outlined caveats in relation to indirect comparisons, this was not reflected in the summary Q&A. The Panel considered that other presentations were relevant to idelalisib and Richter's transformation. The presentation that immediately preceded that on Richter's Transformation, 'Genomic architecture and clonal evolution in **CLL**', included a section entitled 'Clonal Evolution in Richter's transformation'. A preceding presentation 'Idelalisib mechanism of action:Immune mediated-activity and transformation' detailed the product's mechanism of action and, in the Panel's view, highlighted features relevant to prevention of RT and idelalisib. The Panel considered that the overall narrative of the presentations was such that they highlighted features of idelalisib including its unique mechanism of action in relation to the prevention of RT which was described in the final presentation as an unmet clinical need. The Panel considered that the totality of the presentations, together with the description of such comparative data as 'potentially practice changing' by a globally respected expert was such that, on balance, the company advocated the use of idelalisib for prevention of Richter's Transformation. In the Panel's view, relevant caveats should have been an integral and prominent part of each slide in question and such caveats should be accurately reflected in the speaker's comments. In this regard, the Panel was concerned that the presentation had been available to download from the Faculty portal. The Panel considered that the presentations and comments by the speaker went beyond training a speaker to respond to an unsolicited question about a product and RT. In this regard, the Panel noted that a UK existing Faculty member had subsequently delivered promotional presentations which positively referred to idelalisib's mechanism of action in the context of the prevention of Richter's transformation. In the Panel's view, Zydelig was positioned as a preventative treatment for Richter's Transformation as alleged. A breach of Clauses 3.2 and 7.2 was ruled.

In relation to the complainant's allegation about an imbalance of delegates from Italy, the Panel noted Gilead's explanation, including that the product was launched in Italy a few months before the safety signal emerged in March 2016 and Italian clinicians had little experience in managing adverse events at that time. The Panel did not consider that the proportion of Italian participants alone rendered the meeting inappropriate as a training event. No breach of Clause 9.1 was ruled on this narrow point.

In relation to the allegation that Gilead accepted and verbalised the hypotheses about idelalisib being an 'immuno-oncology compound which supresses the high risk clones' without data to support such claims,

the Panel noted Gilead's submission that it had no recollection or record of this being verbalised at the meeting. The Panel noted that the comment, or one closely similar, did not appear in the summary of Q&A. The Panel therefore considered that the complainant, who bore the burden of proof, had not established that the statement had been made and, on this basis, ruled no breach of Clause 7.4 of the Code.

Complaint received **19 April 2018**

Case completed **3 June 2019**
