CASE/0747/09/25

COMPLAINANT v ROCHE

Allegations regarding misleading information on a promotional website

CASE SUMMARY

This case was in relation to a promotional webpage for Alecensa (alectinib hydrochloride) that presented a Kaplan-Meier curve alongside a relative risk reduction claim. The complainant alleged that the relative risk reduction was prominently displayed without also referring to absolute risk reduction which meant the reader had to make the calculation themselves and overemphasised the effect of the medicine.

There was an appeal by Roche of one of the Panel's rulings.

The outcome under the 2024 Code was:

Breach of Clause 6.1 [Panel's breach ruling upheld at appeal]	**Making a misleading claim**

No Breach of Clause 5.1	**Requirements that companies maintain high standards all times**

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

A complaint was received about Roche Products Limited from an anonymous, non-contactable complainant who described themselves as a health professional.

COMPLAINT

The complaint wording is reproduced below:

> "A promotional website for ALECENSA aimed at UK HCPs, contains a graph for the key efficacy endpoint in the ALINA trial. However, the graph prominently displays the Relative Risk Reduction with no accompanying Absolute Risk Reduction, forcing the reader to make the calculation on their own. On first impression, and under time constraints, this overemphasises the effect of ALECENSA to the viewer. I believe this is in breach of clause 6.1. Website accessed (25/9/25)."

When writing to Roche, the PMCPA asked it to consider the requirements of Clauses 6.1 and 5.1 of the 2024 Code.

ROCHE'S RESPONSE

The response from Roche is reproduced below:

> "Roche takes its ethical responsibilities seriously, with adherence to the ABPI Code of Practice forming a core part of this commitment. We were therefore disappointed to receive the above-mentioned case and outline below why we believe the material in question remains fully compliant with the ABPI Code.
>
> The complaint concerns a promotional webpage for Alecensa (alectinib) which is marketed by Roche in the UK for the treatment of adult patients with ALK-positive, advanced non-small cell lung cancer (NSCLC) and for the adjuvant treatment of adult patients following tumour resection for ALK-positive NSCLC in accordance with the Summary of Product Characteristics.
>
> The webpage in question is intended for UK healthcare professionals and presents efficacy data from the ALINA trial. The complainant alleges a breach of Clause 6.1 on the basis that the content displays the Relative Risk Reduction (RRR) without the accompanying Absolute Risk Reduction (ARR), which they suggest could be misleading and may overemphasise the treatment effect. As requested by the PMCPA we also consider Clauses 6.1 and 5.1 in our response.
>
> Clause 6.1 states *'Information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. They must not mislead either directly or by implication, by distortion, exaggeration or undue emphasis. Material must be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine.'*
>
> Furthermore, the supplementary information provides clarity on the requirements for absolute risk (AR) be to clear when presenting relative risk:
> *'absolute risk and relative risk. Referring only to relative risk, especially with regard to risk reduction, can make a medicine appear more effective than it actually is. In order to assess the clinical impact of an outcome, the reader also needs to know the absolute risk involved. In that regard, relative risk should never be referred to without also referring to the absolute risk. Absolute risk can be referred to in isolation'*
>
> In oncology trials, time-to-event data, such as overall survival (OS), progression-free survival (PFS), and disease-free survival (DFS), are considered the gold standard for demonstrating the efficacy of an intervention compared with standard of care. As outlined in the *European Medicines Agency (EMA) Appendix 1 to the Guideline on the Evaluation of Anticancer Medicinal Products in Man – Methodological Considerations for Using Progression-Free Survival (PFS) or Disease-Free Survival (DFS) in Confirmatory Trials* (EMA/CHMP/27994/2008/Rev.1), adopted December 2012 , these endpoints are defined prospectively and analysed using time-to-event methods to ensure

objectivity and minimise bias. Hazard ratios (HR) are therefore used to express the relative reduction in risk of an event over the entire study period, rather than at a single time point.

Alongside the HR, 95% confidence intervals (95% CIs) are used to quantify the imprecision of the hazard ratio, given that trials study the intervention in a relatively small population. Statistical significance is designed around the HR, and not median time to event, or percentage of events at a given time point (e.g. 12 months). Presentation of the HR, 95% CI and p value provide a clear representation to a healthcare professional of the efficacy of the intervention. Healthcare professionals from the UK attend scientific meetings and oncology congresses (e.g. ESMO, ASCO etc.) where the data is frequently presented in this manner, and thus they are familiar with the way of presenting data as was presented on the Roche Resources page for alectinib.

The representation of data in the promotional materials was reviewed extensively with input from our biostatistics team regarding the mathematical differences between hazard ratio, risk reduction, and relative risk. This review occurred during content development and prior to certification to ensure accurate, non-misleading presentation in line with the Code and appropriate to the oncology context.

Mathematically, a relative risk is a presentation of data at a singular time point (e.g. 12 month OS) and is specific to binary endpoints where relative risk is the summary measure. A hazard ratio is the risk of an event in each treatment arm as a distribution of risk over time, it is not by definition a relative risk (*George A et al. Cureus. 2020;12(8):e1004)*. The distribution of risk over time is best represented by the Kaplan-Meier curves themselves. This provides a clear visual representation of the separation of curves allowing the healthcare professional to clearly see differences between the intervention and comparator.

Given these conversations it was concluded that it could be misleading to calculate AR from the HR and corresponding reduction in risk of event, in this case disease-free survival (DFS). To ensure the data presented were clear, in context and would not mislead in terms of overstating efficacy, or data being used without context, the KM curve would be included alongside the HR, 95% confidence intervals, p values, and corresponding reduction in risk of event to allow healthcare professionals to see clearly the full data within the context of the trial, and visually see differences between the intervention (alectinib) and comparator (platinum chemotherapy).

Within the Roche Resources webpage for alectinib, our intent was to highlight the primary analysis of the ALINA trial, ensuring that the HR and reduction in risk of event Disease Free Survival (DFS) were presented in alignment with the published primary endpoints and consistent with how efficacy data are typically displayed in pivotal oncology studies;

'The hazard ratio for disease recurrence or death was 0.24 among patients with stage II or IIIA NSCLC and in the intention-to-treat population, which corresponds to a 76% lower risk with adjuvant alectinib than with chemotherapy' (Wu Y et al. N Engl J Med 2024;390:1265-76).

The presentation of the data on the Roche Resources page included reduction in risk of disease recurrence or death between alectinib vs. platinum-based chemotherapy, was supported by a prominent HR, 95% CI and statistical p value alongside percentage risk information at various timepoints (i.e. month 24 & month 36) clearly marked with 94% vs. 64% and 89% vs. 54%, respectively. It is common practice to add data points on the Kaplan-Meier graphs at specific timepoints e.g. median, 12 months, 2 years, 5 years etc. to aid the audience in interpreting the difference in risk between the different arms given that hazard ratios are continuous. In Roche's case we have presented 2 data points to ensure there is no risk of being misleading. Claims were not made on these individual time points, given the statistical analysis plan of the study was designed to show statistical significance based on the HR and not individual time point data.

Immediately below the claim regarding a reduction in the risk of disease progression or death with alectinib vs. platinum based chemotherapy, a clear and prominent KM curve was included to ensure that healthcare professionals could clearly see the relative hazard reduction over time within the trial. Roche believes that with the information included, the healthcare professional audience would be able to interpret the time-dependent HR and not be misled to the efficacy of alectinib vs. platinum-based chemotherapy.

Furthermore, Roche believes that providing a calculation of absolute risk reduction known to be mathematically incorrect increases the likelihood of confusion to healthcare professionals, and may inadvertently mislead the relationship between HR and reduction in the risk of an event over time.

Broader Industry perspectives on the presentation of Oncology trial endpoints

We note that variation exists, across the industry, on how time-to-event data outputs (e.g. OS, DFS etc.) from oncology clinical trials are presented. Although it may be helpful to healthcare professionals to support their decision-making to have an aligned, consistent method for presenting such outputs, currently one approach does not seem to exist.

To demonstrate these differences, the table below provides several examples of materials created by the pharmaceutical industry for UK healthcare professionals, for products licensed and promoted within Oncology.

These examples demonstrate both an inconsistency of approach across the industry but also show that a number of other companies active within Oncology seemingly also believe the approach Roche has taken with our representation of this data to be acceptable as an industry standard.

[Table containing information on how other pharmaceutical companies present relative and absolute risk reduction]

In summary, Roche strongly refutes a breach of Clause 6.1 on the basis that the efficacy information presented on the Roche Resources page is accurate, balanced, and does not mislead healthcare professionals on the efficacy of alectinib vs. platinum-containing chemotherapy. Presenting the hazard ratio, 95%

confidence intervals, and p value alongside the reduction in risk of disease progression statement, with the Kaplan-Meier curve immediately below the claim ensures healthcare professionals can see the time-dependent nature of the reduction of risk of disease progression across the entire study duration, thereby preventing any overstatement of efficacy at a single time point. As such, Roche also refute a breach of Clause 5.1 maintaining high standards."

PANEL RULING

This complaint concerned a Kaplan-Meier curve and an accompanying relative risk reduction claim made on a promotional webpage for Alecensa (alectinib hydrochloride). The complainant alleged that the presentation of relative risk reduction without absolute risk reduction meant the reader had to make the calculation themselves and overemphasised the effect of the medicine.

The Alecensa webpage was hosted on the Roche Resources website with the graph at issue appearing beneath the subheading "Systemic efficacy" within a section describing the ALINA trial. The section included the claim "ALECENSA significantly reduced the risk of disease recurrence or death by 76% compared with platinum-based chemotherapy (HR=0.24 [95% CI: 0.13, 0.43])" together with a Kaplan-Meier curve that displayed disease-free survival (%) over time (months) for the intention-to-treat population (Stage IB–IIIA) based on a clinical cut-off date of June 2023.

Positioned directly above the KaplanMeier curve was a large, prominent callout graphic displaying "76% reduction in the risk of relapse with Alecensa vs chemotherapy". Landmark disease-free survival rates were illustrated on the curves for Alecensa compared with chemotherapy at 24 months (94% vs 64%) and 36 months (89% vs 54%). The hazard ratio, 95% confidence interval, and p-value were displayed in a prominent box overlaid on the lower portion of the graph ("HR=0.24; 95% CI: 0.13, 0.43; p<0.001") and a table illustrating the number of patients at risk was provided beneath the graph.

The Panel noted Roche's submission that, in oncology trials, time-to-event endpoints such as disease-free survival were considered the gold standard for demonstrating efficacy. Roche submitted the hazard ratio expressed the relative reduction in risk over the entire study period, rather than at a single time point, but was "not by definition a relative risk". In this regard, Roche stated that "mathematically, a relative risk is a presentation of data at a singular time point (e.g. 12-month OS [overall survival]) and is specific to binary endpoints where relative risk is the summary measure".

Roche submitted that calculating an absolute risk reduction from a hazard ratio could be misleading and that the inclusion of the Kaplain-Meier curve, together with the hazard ratio, 95% confidence interval, and p value, enabled health professional to visually interpret the full data and treatment effect over time between the two arms.

The Panel acknowledged that hazard ratios and Kaplan-Meier curves, amongst other measures, were standard approaches for presenting time-to-event data and that the intended audience would be familiar with the way in which the data was presented.

However, the Panel noted that Clause 6.1 required, amongst other things, that information, claims and comparisons must not mislead, either directly or by implication, by distortion,

exaggeration or undue emphasis and that material must be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine. The supplementary information to Clause 6.1 stated:

> "Referring only to relative risk, especially with regard to risk reduction, can make a medicine appear more effective than it actually is. In order to assess the clinical impact of an outcome, the reader also needs to know the absolute risk involved. In that regard, relative risk should never be referred to without also referring to the absolute risk. Absolute risk can be referred to in isolation"

The Panel took into account the hazard ratio (HR=0.24) was presented within the graph and that the treatment effect had been presented as a risk reduction through the large claim "76% reduction in the risk of relapse with Alecensa vs chemotherapy", positioned prominently above the graph.

While the Panel accepted that the Kaplan-Meier curve included two data points to aid the interpretation in risk difference and that a table presenting number of patients at risk was provided, the Panel considered that the presentation of risk reduction without absolute risk reduction meant the webpage was not sufficiently complete to allow the reader to make an immediate assessment. The Panel further accepted that the prominent presentation of risk reduction, in isolation, might overemphasise a medicine's effects. In the absence of accompanying absolute risk reduction information, the Panel ruled a **breach of Clause 6.1**.

The Panel noted Clause 5.1 required companies to maintain high standards at all times. In the Panel's view, the complainant's concerns had been adequately covered by its ruling under Clause 6.1. In the absence of any other allegations, the Panel did not consider it had been established that there was a failure to maintain high standards. The Panel ruled **no breach of Clause 5.1.**

APPEAL BY ROCHE

Roche's written basis for appealing is reproduced below:

> "The Panel ruled a breach of Clause 6.1 due to the absence of accompanying absolute risk reduction information. Roche respectfully disagrees with the ruling on the basis that the Kaplan-Meier (KM) curves provide a continuous visual record of the absolute risk (AR) over the duration of the study. Hazard Ratios (HR) and KM curves are the standard way of presenting time-to-event data in oncology trials. The target audience for Alecensa (alectinib) consists exclusively of oncology healthcare professionals, and any oncologist viewing the KM curves in question would readily understand the absolute and relative impact of the two treatments on patients in the trial at any chosen time point. Roche therefore submits that the data, as presented, would not mislead the intended audience.
>
> Roche have accurately stated that the reduction in risk of disease recurrence or death is 76%. This refers to the Primary Study Endpoint which Roche is required to report to allow our promotional materials to be properly understood. This is not a relative risk, but an inverse of the HR*, and there is no single corresponding absolute risk reduction

figure that can appropriately summarise the treatment effect across the duration of the study.

*Hazard ratios and relative risk are distinct statistical measures. Hazard ratios reflect differences in event rates over time, whereas relative risk compares event proportions at a fixed time point. In oncology trials, where event risk varies across the duration of a study, hazard ratios and Kaplan–Meier curves are standard methods for presenting time-to-event outcomes.

The supplementary information to Clause 6.1 in the Code specifies that *'Referring only to relative risk, especially with regard to risk reduction, can make a medicine appear more effective than it actually is. In order to assess the clinical impact of an outcome, the reader also needs to know the absolute risk involved. In that regard, relative risk should never be referred to without also referring to the absolute risk'.* Roche notes that the Code does not specify the required format in which AR must be presented. Roche maintains that calculating a single AR figure from the HR or resulting reduction in risk of an event across the trial period, would not appropriately reflect the nature of time-to-event analysis. By contrast, the KM curve presented immediately adjacent to the efficacy statement illustrates the absolute progression rates for both treatments throughout the study period and additionally highlights representative time points at 24 and 36 months. The Panel considered *'the presentation of risk reduction without absolute risk reduction meant the webpage was not sufficiently complete to allow the reader to make an immediate assessment'*. However, Roche submits that the KM constitutes the required reference to absolute progression risk, clearly illustrating the absolute difference in outcomes between the two treatments and thereby satisfying the requirements of the Code. Roche further disagrees that presenting the data in this way requires healthcare professionals to "calculate" the absolute treatment effect; the KM curves are a standard and readily interpretable visual representation within the oncology community. Roche note that several pharmaceutical companies with expertise in oncology present time-to-event data using the same approach taken in the Alecensa promotional website.

The Panel stated '*the prominent presentation of risk reduction, in isolation, might overemphasise a medicine's effects'*. Roche disagrees that the statement (76% reduction in the risk of relapse with Alecensa vs. Chemotherapy) was presented in isolation. The KM curves, including the "No. of patients at risk" and specific percentage points at 24 and 36 months allows clinicians to readily understand the absolute improvement in the likelihood of remaining cancer-free compared to the standard of care. Roche submits that the information presented does not overemphasise the effect of Alecensa and notes that the Panel ruling does not identify how the presentation would in fact mislead the intended specialist audience.

In summary, Roche submits that the totality of information provided on the Alecensa webpage allows the reader to clearly understand:

i. The pivotal clinical trial primary outcome, as presented in the Summary of Product Characteristics;
ii. The relative efficacy of alectinib in preventing disease progression relative to the control treatment; and

iii. The absolute risk of disease progression with both treatments and the difference between the two treatments with regard to this metric.

Roche believes the material does not mislead and is sufficiently complete to enable readers to form their own opinion of the therapeutic value of the medicine.

Roche would be grateful if the Appeal Board would reconsider the ruling of the Panel in relation to the breach of Clause 6.1."

APPEAL BOARD RULING

The Appeal Board understood that the claim, "76% reduction in the risk of relapse with Alecensa vs chemotherapy", was derived from the inverse of the hazard ratio and reflected a reduction in the event rate over the study period rather than risk. Nonetheless, the Appeal Board considered the claim in the form in which it was presented to readers, as a risk reduction, and assessed it on that basis.

The Appeal Board accepted that hazard ratios and Kaplan-Meier curves were established methods of presenting time-to-event data and that the intended audience would be familiar with their interpretation. The Appeal Board further accepted that the Kaplan-Meier curve presented the absolute risk over time, from which the absolute risk reduction could be derived.

The Appeal Board nevertheless considered the manner in which the claim had been presented. Clause 6.1 required that information, claims and comparisons must, among other things, not mislead either directly or by implication, by distortion, exaggeration or undue emphasis. The claim in question presented the 76% risk reduction prominently in large, bold red font, whereas the absolute risk reduction was not stated and needed to be calculated from the Kaplan-Meier curve. The Appeal Board considered that this gave undue emphasis to the risk reduction claim and had the potential to mislead in this regard. The Appeal Board therefore upheld the Panel's ruling of a **breach of Clause 6.1**. The appeal was unsuccessful.

Complaint received **25 September 2025**

Case completed **5 August 2026**