cohort treated with eight and six cycles, respectively. Consistently, no evidence of a difference was observed in a multivariate analysis [HR with six cycles: 0.88 (95% CI: 0.54–1.44); $P = 0.62$].

Additionally, no evidence of a difference in outcome according to use of six or eight cycles of R-CHOP-21 were observed in subgroup analyses stratified according to age ≤/>70, low- and high-risk IPI score, and excluding patients treated with consolidative radiotherapy.

These results are in line with results from the Eastern Cooperative Oncology Group/Cancer and Leukaemia Group B 9703 study, where the outcome of patients who received six cycles of R-CHOP-21 were comparable to those of patients with similar patient characteristics treated with eight cycles in the GELA study [1, 2].

The RICOVER-60 trial demonstrated increased toxicity in absence of improved outcome with eight compared with six cycles of R-CHOP-14 [5]. However, only elderly patients (aged 60–80 years) were included and a similar comparison of R-CHOP-21 has not been carried out. Thus, the present study contributes valuable data regarding the use of six cycles of R-CHOP-21 among patients of all ages and risk groups.

In summary, we note that the majority of patients with DLBCL treated with R-CHOP-21 during the surveyed time period received six cycles, and conclude that outcomes following six or eight cycles of R-CHOP-21 for newly diagnosed DLBCL are comparable in terms of efficacy.

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Reply to the letter to the editor: 'The hard road to patient-centered care: 3 or 6 months of adjuvant chemotherapy for patients with stage III colon cancer?' By P. Trendsz et al.

P. Trensz et al. [1] in their Letter to the Editor of *Annals of Oncology* discussed our Special Article, a meeting report addressing 'The hard road to data interpretation: 3 or 6 months of adjuvant chemotherapy for patients with stage III colon cancer' [2].

They cite a sentence of our conclusion where we state that 'the main driver for the duration of adjuvant treatment were treatment choice and very importantly the patient's attitude to his/her disease'.

In the IDEA project, the pooled analysis showed that a reduced duration of adjuvant chemotherapy was associated with an important reduction of long-term toxicity whereas the 3-year DFS difference was very small with no 'clinically significant' reduction. This may, however, matter for an individual patient and should be clearly explained and discussed with each individual patient. P Trendsz et al. consider this situation as a 'clinical equipoise'. This would be correct if there were some degrees of uncertainty but the efficacy is clinically preserved (absolute difference in 3-year DFS is 0.9% on 13 000 patients) when the toxicity is highly significantly reduced in IDEA.

We fully agree, with these results in mind, that clear information on the Pros and Cons has to be discussed with the patient for him to be part of the final choice in terms of treatment duration. Based on a limited-size poll of 45 colon cancer patients, one-third of patients would have chosen to accept a reduction of 1%–2% in cure rate only and two-third a risk reduction of >2%: based on their response they were retrospectively grouped in 'fighters' (risk of 1%–2%) or 'fatalists' accepting a higher risk for a benefit of reduced toxicity. P Trendsz et al. consider that the 'chosen metaphor' is inappropriate and might influence decision making,

inducing a feeling of guiltiness. The terms of 'fighters' or 'fatalists' were used to group the patients (it was more convenient than A and B) for the discussion of the panel and does not imply a judgement on the patient's individual choice, that in all cases is to be respected. The authors misunderstood our intention when they state, 'The main decision . . . should be the patient rather than predefined patient's attitude'. The attitude is not predefined and the choice made after a clear information and discussion with the patient, to answer and clarify possible questions. The groups of 'fighters' and 'fatalists' were built a posteriori for the sake of the discussion. The decision is never made by the oncologist only, but should emerge from a frank patient/doctor relationship and dialogue where the patient's personal preferences and values are the final drivers of the choice.

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Anti-EGFR therapy in oesophagogastric cancer: precise but not enough

A recently published article in *Annals of Oncology* reported an umpteenth negative trial investigating anti-epidermal growth factor receptor (EGFR) treatment in oesophagogastric (OG) cancer. Indeed, although Ruhstaller et al. [1] demonstrated a significant improvement in loco-regional control from the addition of cetuximab to multimodal treatment in resectable oesophageal cancer, the study did not meet its primary survival end points. These results are added to an ever-growing number of anti-EGFR negative trials in molecularly unselected OG, including RTOG0436 and SCOPE1 (with cetuximab) in non-metastatic oesophageal cancer, REAL-3 (with panitumumab) and EXPAND (with cetuximab) in untreated advanced gastric cancer and COG (with gefitinib) in pre-treated advanced oesophageal cancer. Based on that, it is legimate wondering whether the anti-EGFR story in OG will ever have a happy ending.

EGFR overexpression and amplification occur in 27%–55% and 4%–14% of OG, respectively, and are thought to mediate a more aggressive oncogenic phenotype [2, 3]. Specifically, EGFR amplification has been reported to be more common in junctional tumours and stage IV disease [4].

In patient-derived xenografts of OG treated with cetuximab, all responding patients had ≥4 EGFR gene copies and those with the highest copy number displayed the highest chance of benefit [5]. Moving to the clinic, although the abovementioned trials failed to demonstrate an improvement in OS, patients' population were not enriched neither for positive predictive factors (e.g. EGFR) nor negative predictive factors (e.g. RAS mutation). More interestingly, post hoc analyses suggested that a small subset of OG exists that may benefit from EGFR-directed therapy. A biomarker analysis of the EXPAND study showed that higher EGFR expression assessed by immunohistochemistry correlated with improved OS, PFS and tumour response in patients receiving cetuximab. Accordingly, in a correlative molecular analysis of the COG trial, EGFR-amplified patients (7.2%) derived the greatest benefit from gefitinib (HR 0.21, $P = 0.006$, 4.17 versus 1.70 months).

Very recent evidence prospectively supports anti-EGFR treatment in EGFR-amplified GC. Maron et al. [4] showed an overall response rate of 57%, a disease control rate of 100% and a median PFS of 10 months for a subgroup of 7 EGFR-amplified (≥8 copies) patients, identified after screening 140 stage IV OG cases over a 27-month period. Bearing in mind all the caveats related to the tiny sample size and heterogeneous treatment modalities, this study offers a promising proof of concept regarding the selection and the targeting of EGFR-driven OG.

Despite negative results so far attained, it seems that a subgroup of molecularly highly selected OG could benefit from anti-EGFR therapy. Notably, in view of the worldwide burden of OG and the rising incidence of junctional OG, these numbers are not negligible. Following previous success in other cancer types, such ALK in lung cancer, it is desirable that collaborative efforts would be set up to ascertain the real value of a 'targeted agent in a targeted population'. Next-generation clinical trials using expansion platform design provide a proper tool to address the issue of low-incidence druggable genomic aberrations. This appears as the most reasonable road to get closer to the goal of precision and personalized medicine in OG.

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