In addition, the authors defined objective tumor response as complete response (CR) and partial response (PR) in this article, quite different from the definition in their previous article, which excluded the complete response (CR) with the reason that patients with complete response (CR) following the first TACE did not receive a further TACE session. We wonder whether the patients with complete response (CR) after TACE-2 or TACE-3 received further TACE sessions in their institutions. We suppose that the distinct definitions of objective tumor response may diminish the credibility of their study. All the above demonstrates that the ART score is not as validated as we previously supposed. All in all, further study is needed to fully validate the clinical practice of ART-score regardless of its remarkable significance in helping distinguish patients who will benefit from repeated TACE.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

Reply to the Letters to the Editor regarding the sequential ART-Score

To the Editor:

We would like to thank Yousuf and colleagues for the thoughtful comments on our work regarding the sequential use of the ART score to select patients for retreatment with TACE [1]. They are right in commenting that the Child-Pugh score (CPS) consists of 5 variables but the reason why we use the change in CPS was that in our uni- and multivariate analysis from the original ART-score manuscript, the change in composite CPS was a better predictor for survival than the change in the individual variables included in the CPS [2]. In addition, from a practical point of view, the CPS has to be calculated to evaluate the patient’s suitability with regards to liver function for the selection for any treatment

References


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according to the BCLC staging classification, so this information is always available anyways. We also agree that the greatest weight in the ART-score is put on the aspartate aminotransferase (AST) and not on radiologic response. But this was derived from the hazard ratio in the multivariate analysis giving the greatest weight to the rising AST as opposed to other statistically significant parameters.

We acknowledge that the authors developed the HAP score [3], but the HAP score serves a different purpose: it is a prognostic score, which helps to subclassify BCLC-stage B patients undergoing chemoembolization into different prognostic groups prior the first TACE treatment. In contrast, the ART-score, aims to detect (1) patients that can tolerate repeated-TACE well and (2) patients, whose liver function and prognosis would be harmed by another occlusion of the arterial blood supply to parts of the liver. So patients might be in a good prognostic group by the HAP score or by the BCLC stage B subclassification at baseline, but a subgroup of these patients may present with an ART of \(\geq 2.5\) points prior to TACE-2 with subsequent dismal prognosis in case of retreatment with TACE. On the other hand, some suboptimal candidates for TACE at baseline may tolerate repeated TACE quite well as outlined by an ART score of 0–1.5 points and therefore have a fairly good outcome with TACE treatment, as detailed in our original ART-score manuscript.

Regarding the comments by Han and colleagues we would like to confirm that even if a patient receives 2.5 points in the ART-score through lack of radiologic response and an increase in CPS by 1 point after TACE 1, he still is a poor candidate for further TACE’s. It might be true that he might show a radiologic response after the second TACE but this will lead to further deterioration in his liver function and therefore a dismal prognosis despite radiologic response. This has been clearly shown in our initial art score manuscript. Therefore the recommendations by different authors that patients should undergo at least two TACE-procedures initially – statements made well before the publication of the art score – cannot be supported anymore.

Regarding the impact of different TACE or TAE techniques, the authors misunderstood the message we are giving: it might be true that treatment with DC-beads gives a better treatment respond than cTACE (even though not supported by the published literature so far [4]), but this will be taken into account by the ART-score anyway through the parameter “radiologic response”. Thus, different TACE techniques could have an impact on the ART-score values; but nevertheless, the ART-score values obtained retain their prognostic significance regardless of the technique used.

We disagree with the authors that the response definition is different because we did not evaluate patients with complete response in our initial ART-score manuscript: the definition was the same but the inclusion criteria did not allow inclusion of patients with less than 2 TACE-procedures (which was obviously necessary to evaluate the impact of repeated TACE’s on outcome, since patients with complete response do not receive retreatment with TACE within three months if TACE is applied in a “on demand” fashion). Patients that had a complete response after TACE 2 or TACE 3 did not receive further TACE sessions in our institutions, as outlined very clearly in the methods of our manuscripts. So the validation of the ART-score seems to be very robust but we certainly welcome further evaluation of the ART-score in different patient populations worldwide, in particular when performed prospectively.

Conflict of interest

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Triple or dual therapy for HCV-1 naive patients?
Optimizing selection tools

To the Editor:

We read with interest the paper by Andriulli et al. [1] about the identification of naïve HCV-1 patients who can be treated with dual therapy according to baseline and on-treatment parameters.

Important predictive factors of sustained virological response (SVR) are the IL28B single-nucleotide polymorphisms (SNPs), however the authors considered only the rs12979860 SNP, forgetting the more important rs8099917 [2–4]; this is, in our opin-