Implementing a novel method to estimate the "Burden of Therapy" (BOTh) for patients with metastatic pancreatic cancer treated with gemcitabine plus afatinib vs. gemcitabine in the AIO ACCEPT trial.

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Background:

The phase II ACCEPT trial included 119 patients (pts) with histologically proven pancreatic cancer without any previous systemic treatment for metastatic disease. Pts were randomized in a 2:1 ratio to receive either afatinib 40mg orally once daily + gemcitabine (1000mg/m^2 iv weekly for three weeks followed by one week of rest, repeated every four weeks) or gemcitabine alone. The addition of afatinib did not lead to improved efficacy (7.3 vs. 7.4 months, HR 1.06, p = 0.80; data previously shown). The traditional analysis of adverse events was not able to reveal the actual patient's burden in each of the treatment arms.

Methods:

BOTh^{Tox} is a highly sensitive, novel methodology utilizing patient-level data to derive a quantitative estimate for the "Burden of Therapy/Toxicity" (BOTh) that all or individual pts experience on each day of a clinical study[1]. The daily burden estimate is based on number and severity of adverse events (AEs) that occur contemporaneously and consecutively, in a combination of incidence and severity resulting in a major advantage over current methods. A chart displays the total burden experienced by pts on each day throughout the study and statistical analyses are performed with the area under curve.

Results:

The BOTh^{Tox} analysis revealed that the daily burden of toxicity for pts in the gemcitabine-alone arm was 6.8 compared to 11.5 in the combination treatment arm ($p = 0.0005$). However, the day to day variation in burden was higher in the gemcitabine-alone arm. The higher burden in the combination arm was already visible at a very early stage of the trial when most pts were still on treatment.

Conclusions:

Whereas the traditional analysis of AEs only gave a static interpretation, BOTh^{Tox} revealed a more dynamic view on burden of toxicity on pts taking single vs combination medication in a 200 day time frame. BOTh^{Tox} can facilitate better informed treatment selection.

[1]Abdulahad A. et al. Contemporary Clinical Trials Communications 4 (2016) 186-191.

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