SIOG 2017 - Abstract Submission

Track 1: Solid tumours in the elderly and basic science

Colorectal & GI cancers

O16

NORDIC9: A NORDIC RANDOMIZED PHASE II TRIAL EXPLORING TREATMENT STRATEGIES OF OLDER PATIENTS WITH METASTATIC COLORECTAL CANCER; RESULTS OF A PREPLANNED SAFETY ANALYSIS

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Introduction: Colorectal cancer is a disease of the older but knowledge about treatment strategies among these patients (pts) is sparse as this population is underrepresented in clinical trials[1].

S-1 is a well-tolerated oral 5-FU prodrug[2] and a good alternative in older mCRC pts. Attention may though be focused on kidney function, as a previous study (SOFT)[3] has shown an increased incidence of grade 3-4 diarrhea in patients with a creatinine clearance < 70 ml/min compared to patients with creatinine clearance ≥ 70 ml/min (21% vs. 6%).

Objectives: The overall aim of the NORDIC9 trial is to add knowledge on how to select the optimal treatment for older mCRC pts, who are not candidates for standard combination therapy.

Methods: Older (≥ 70 years) mCRC pts, who are not candidates to full-dose combination therapy, are randomized to:

- *Arm A: Full dose monotherapy* (S-1 30 mg/m^2 po bid day 1-14 q3w, followed by second line irinotecan) or
- *Arm B: Reduced dose (80%) combination therapy* (S-1 20 mg/m^2 po bid day 1-14 + oxaliplatin 100 mg/m^2 iv day 1 q3w, followed by reduced S-1 + irinotecan).

Bevacizumab (7.5 mg/kg iv) may be added at the discretion of the treating clinician.

Geriatric screening tools (G8, VES-13, Timed-Up-and-Go, and Hand Grip strength), Charlson Comorbidity Index, and Quality of Life are evaluated at baseline. Blood samples and tumor tissue are prospectively collected.

Primary endpoint is progression-free survival. Secondary endpoints are overall survival, response rate and correlations between the geriatric screening tools and toxicity as well as efficacy.

Results: A preplanned safety analysis was performed when 50 pts had received 3 cycles. 12 pts received bevacizumab. Median age was 79 (range 70-88) years, 24 pts were female, performance status was 0 (43%), 1 (38%) or 2 (19%). Five (10%) pts discontinued therapy after only 1 cycle due to toxicity (n=2) or PD/clinical deterioration (n=3); 45 pts (90%) continued therapy beyond 3 cycles. Pts receiving only 1 cycle had numerically a worse G8 and VES-13 score.

Grade 3-4 non-hematological toxicity was fatigue (6%), diarrhea (10%), nausea (4%) and vomiting (6%), and was experienced by 10 pts, 6 of them received ≥3 cycles of treatment. Grade 3-4 diarrhea was more frequent (16% vs. 4%) in pts with slightly reduced kidney function (calculated GFR ≤ 70 ml/min) compared to pts with normal kidney function (calculated GFR > 70 ml/min). There was no hand-foot-syndrome, cardiac or hematological grade 3-4 toxicity.

Conclusion: The safety analysis shows acceptable toxicity. 10% of the pts received only 1 cycle of treatment and these pts had worse G8 and VES-13 score.

The NORDIC9 trial continues according to the original design as recommend by the safety committee. Enrollment was initiated March 2015. June 2017, 142/160 pts are included.

EudraCT nr. 2014-000394-39.

References: 1. Papamichael et al. Treatment of colorectal cancer in older patients: International Society of Geriatric Oncology (SIOG) consensus recommendations 2013. (2015) Ann Oncol 26:463-76

2. Winther et al. Experience with S-1 in older Caucasian patients with metastatic colorectal cancer (mCRC): Findings from an observational chart review. (2016) Acta Oncol 55:881-5

3. Yamada et al. Leucovorin, fluorouracil, and oxaliplatin plus bevacizumab versus S-1 and oxaliplatin plus bevacizumab in patients with metastatic colorectal cancer (SOFT): an open-label, non-inferiority, randomised phase 3 trial. (2013) Lancet Oncol 14:1278-86

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