Actv results of the GATTO study, a phase Ib study combining the anti-TA-MUC1 antibody Gatipotuzumab with the anti-EGFR Tomuzotuximab or Panitumumab in patients with refractory solid tumors

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Abstract

Background: The phase I GATTO study explored the feasibility, tolerability and preliminary activity of combining Gatipotuzumab (GAT), a novel humanized monoclonal antibody binding to the tumor associated epitope of mucin 1 (TA-MUC1), and an anti-EGFR antibody. Preliminary evidence suggests a complex interaction between TA-MUC1 and EGFR in the context of epithelial cancers and dysplasia, and partially resistant cell-activity with the double targeting

Methods: In 30 patients with refractory metastatic disease were treated with GAT at 1400 mg Q2W in combination with the glycoengineered anti-EGFR antibody Tomuzotuximab (TO) at 1200 mg Q2W. Due to the risk of infusion related reactions, three cycles of TO were given before start of combination treatment with GAT. After this period patients were split into IO (12 cycles of GAT+TO) or IO-II (3 cycles of GAT+TO + 9 cycles of TO only). Evaluation at 6 and 12 cycles of combination treatment showed colon cancer (CC) already treated with anti-EGFR antibodies, non small cell lung cancer (NSCLC), head and neck breast cancers received TO and GAT administration at the same doses, with SAF treatment starting already one week after the first dose of the anti-EGFR. All studies in the study expansion. Panitumumab (PAN) was used in place of TO in CC patients at investigator’s choice

Results: In the final analysis (January 2016) 30 patients were enrolled, and 20 received at least one cycle (96%) with GAT and anti-EGFR antibodies. Safety was overall good and results are required in a separate report. As anticipated in the treatment expansion, activity results of the two parts of the study are demonstrated as promising. There were 2 and 1 objective partial responses in the first and second part of the study, all in CC patients. In the expansion phase, the median Progression Free Survival (PFS) of CC patients who received TO (16.5) and PAN (9) was 1.5 ± 2 months, respectively. There were 2 responses in each subgroup, and the duration of response was 3.4 ± 2.7 months in patients treated with TO, and 1.1 ± 1.2 months in patients treated with PAN. The PFS @ 6 and 12 months were 3.3 and 6.7 months respectively, and 1.3 and 2.3 months respectively. These results may be an indication of survival benefit at high risk CC patients. The high safety profile included only 1 GAT and 6 TO related adverse events, and these were not related to the study treatment of NSCLC, head and neck breast cancers received TO and GAT administration at the same doses, with SAF treatment starting already one week after the first dose of the anti-EGFR. All studies in the study expansion. Panitumumab (PAN) was used in place of TO in CC patients at investigator’s choice

Conclusions: Combination of TA-MUC1 and EGFR targeting activity is safe and feasible. Interesting anti-tumor activity was observed in heavily pretreated CRC and NSCLC patients. The good safety profile is also expected to allow combination in future studies with established chemotherapy treatments such as Irinotecan, Docetaxel or Pemetrexed, potentially broadening treatment options for late stage mCRC or NSCLC patients.

Rationale and Methods

Gatipotuzumab (GAT) is a novel humanized monoclonal antibody, recognizing the tumor-associated epitope of mucin 1 (TA-MUC1). A low affinity glycosylated MUC1 (GAT) is a second-generation anti-EGFR antibody. As the complex interaction between TMS-TA and TA-TM expressed on the tumor cell surface has been demonstrated to drive carcinogenesis DB, a Phase I trial combining Gatipotuzumab and an anti-EGFR antibody has been conducted in patients with refractory solid tumors.

Phase Ib, open label, multicenter (5 centers in Germany, Spain and Italy)

Primary phase: Tomuzotuximab (TO) treatment (1200 mg/m² every 2 weeks after 3 doses of TO; 1200 mg/m²/wk) Extenion phase: GAT treatment (520 mg/m²/day) started 1 week after TO (1200 mg/m²/wk) or placebo

The primary population for safety and efficacy analyses was the treatment combination population including all patients who received treatment at least once with both antibodies (Tomuzotuximab / Panitumumab / Gatipotuzumab).

Primary phase: 20 patients

- mOS at 3 mo = 66.6 months
- mPFS at 6 mo = 22.2 months
- PR in 2 patients, ORR 10.0%

Extension phase: 30 patients

- mOS at 6 mo = 81.8 months
- mPFS at 6 mo = 42.4 months
- PR in 5 patients, ORR 16.7%

Activity results of study phase

Results in extension phase mCRC patients

Primary phase: mPFS: 10.0 months

- mOS at 3 mo = 60.0\%
- mOS at 6 mo = 43.6\%
- DOR, mPFS, and ORR were numerically higher in the PMS group compared to the Tomuzotuximab group

Conclusions

Combination of TA-MUC1 and EGFR targeting antibody is safe and feasible. Interesting anti-tumor activity was observed in heavily pretreated CRC and NSCLC patients.

The good safety profile is also expected to allow combination in future studies with established chemotherapy treatments such as Irinotecan, Docetaxel or Pemetrexed, potentially broadening treatment options for late-stage mCRC or NSCLC patients.

Baseline STA-MUC1 levels show promise as a predictive biomarker for efficacy outcome.

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