**Long-term outcome of dasatinib first-line treatment in gastrointestinal stromal tumors: A multicenter two stage phase II trial SAKK 56/07**

**Background:**
Tyrosine kinase inhibitors (TKIs) have improved the outcome of patients (pts) with gastrointestinal stromal tumor (GIST), but most patients eventually develop resistance and progress. Dasatinib is a potent inhibitor of bcr-abl, kit and src-family kinases, and imatinib resistant cells, providing the rationale of this trial. Evaluation of GIST treated with TKIs is routinely done by computed tomography (CT). 18F-fluorodeoxyglucose positron-emission-tomography (FDG-PET) measures tumor metabolic activity for early response assessment and outcome prediction.

**Methods:**
This two-stage phase II trial investigated dasatinib in pts with TKI-naïve GIST. Dasatinib starting dose was 2x70mg/day in pts with histologically proven, FDG-PET positive GIST. Response evaluation was done by serial CT and FDG-PET using EORTC PET response criteria (Young et al. 1999). Elective surgery was allowed after 6 months of trial treatment. Primary endpoint was response (CR+PR) by FDG-PET after one month of dasatinib. In case of progression the treatment was changed to imatinib.

**Results:**
47 of 52 planned pts had been enrolled from December 2007 to November 2011, when the trial was terminated due to slow accrual. 42 pts were eligible. Median age was 61 years, 24 pts were male, 18 female. Performance status was 0 in 29 and 1 in 13 patients. Median follow-up (mFU) was 47.7 months. Pts went off trial for elective surgery (n=8), after 26 cycles as per protocol (n=5), progression (n=14), toxicity (n=7), other (n=5) and three patients died (two off-drug, one on-drug). Toxicity was most often gastrointestinal or pulmonary, G4 was observed in 5% of pts, and G3 in 48% of pts. Dose was interrupted or reduced in 25% of cycles. The primary endpoint, FDG-PET response rate (CR+PR) at 4 weeks was 74% (14 CR, 17 PR, 6 SD, 3 PD, 2 not evaluable). Median progression-free survival (mPFS) is 13.6 months and median overall survival (mOS) has not been reached yet.

**Conclusions:**
Dasatinib shows high metabolic response rates in TKI-naïve pts with FDG-PET positive GIST. Median PFS was 13.6 months and 74% alive at 4 years (CI: 60-95%).

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