### Dasatinib first-line treatment in GIST: Multicenter phase II trial of the SAKK (SAKK 56/07)

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#### Summary

- **Objective(s):**
  - Primary objective: Efficacy and safety of dasatinib in GIST
  - Correlation of dasatinib efficacy with mutational status

- **Secondary objective(s):**
  - Efficacy and safety of dasatinib in GIST

- **Starting dose is 70 mg BID (one cycle = 4 weeks)
- Dose level: 1 - 50 mg BID
- Dose level: 2 - 100 mg BID
- Continue until progression, unacceptable toxicity and up to 2 years
- After 2 years, decision of the physician (continue or switch)
- Elective surgery is allowed after 6 cycles if SD or better
- Adjuvant Treatment to be considered
- Interim analysis (response + toxicity) after 6-12 pts

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- **Adverse Events per Patient**

- **Survival (Secondary Endpoint):**
  - Median Follow-Up: 13.4 months
  - On trial: 15 pts (35%)
  - Off trial: 26 pts (65%)
  - Median OS: not reached

- **PET Response (Primary Endpoint):**
  - SUV-R final assessment PET at 4 weeks compared to baseline
  - CORTIC criteria (Young et al EJC 1999)
  - PET Response Rates (CR+PR) (95% CI)
    - Overall: 72% (44–94%)
    - Kit Type: 57% (18–86%)

- **Central Review**
  - Evaluation surgery allowed after month 6
  - Elective surgery allowed after month 6

- **Patient Characteristics**
  - Median age: 50 (range: 21–78)
  - Male: 28 (66%)
  - Performance status 0: 25 (58%)
  - Performance status 1: 7 (16%)

- **Main Exclusion Criteria**
  - Previous therapy against GIST with TKI
  - Previous malignancy within 5 years
  - Clinically significant cardiovascular disease
  - Concurrent medications that interfere with TKIs or are not allowed after TKI treatment
  - Patients with significant general medical condition
  - Active infection
  - *Informed consent*

- **Safety / Toxicity:**
  - Treatment was interrupted in 18 patients: 54%
  - Discontinuation: 5 (50%)
  - Treatment was stopped due to toxicity in 4 patients (10%)
  - 38% of pts experienced a G3, 5% a G4 toxicity
  - 3 deaths occurred

- **Histopathology:**
  - Fluorodeoxyglucose (18F-FDG) PET/CT was centrally reviewed within 3 working days

- **PET-CT**
  - PET: Central Review
  - Pathology: Central Pathology Review and Metabolical Analysis

- **Trial Population**
  - Trial open from 27.01.2008 – 16.11.2011 (early closure: time-out)
  - 67 pts included (12 pts already planned)
  - 6 pts not evaluable: CR-PR not defined (PET failure), regrowth (n=2), baseline CT not available (n=1), baseline CT not available (n=1)
  - 64 pts treated in 11 centers in 8 European countries
  - Total 326 cycles administered (median 6, min 1, max 25)
  - Median follow-up: 12.6 months

- **Key Adverse Events**
  - Diarrhea: 10 (25%)
  - Vomiting: 7 (17%)
  - Nausea: 4 (10%)
  - Nausea, vomiting: 2 (5%)
  - Diarrhea: 10 (25%)

- **Adverse Events per Patient**

- **Potential Connections:**
  - Protein tyrosine kinase inhibitor standard care in advanced GIST
  - Dasatinib as multi-target kinase inhibitor
  - Imatinib or sunitinib failure
  - PET/CT with [18F]-FDG PET/CT
  - Progression by visual analysis
  - Diagnosis of GIST

- **Written consent**

- **Written informed consent before registration.

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