SECOND LINE TREATMENT IN EXON 11 MUTATED GIST PATIENT: IMATINIB DOSE ESCALATION OR SUNITINIB? RETROSPECTIVE ANALYSIS OF A MULTI-INSTITUTIONAL EXPERIENCE

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Background

There is a large consensus about the role of both Imatinib dose escalation and Sunitinib as second line therapy in advanced GIST patients. Since imatinib 800 mg is often preferred as a first line treatment in patients harbouring exon 9 KIT mutation, sunitinib remains the only possible second line. Conversely, there is no consensus about the best second line in patients with exon 11 KIT mutation. The second line choice in these subgroup of patients is up to the physician, who relies often on personal experience and patient’s related clinical factors (i.e. response to first line).

Patients and methods

123 exon 11 mutated advanced GIST patients treated in four reference centres were included in the present retrospective analysis. All patients progressed on imatinib 400 mg/die as first line therapy and received, on discretion of physician, a second line treatment with either imatinib 800 mg/die or sunitinib (50 mg/die 4 weeks on/2 weeks of or 37.5 mg/day continuous daily dose).

The type of exon 11 mutation was recorded (deletion versus others) and correlated with both survival endpoints and response according to RECIST or CHOI criteria.

Patients’ features

Median age in our population was 58 years (range: 35-81); 68 (55%) patients were male and 55 (45%) were female. 26 (21%) patients received adjuvant Imatinib after surgery.
No differences in basal clinical and pathological features were identified between the group of patients treated with Imatinib and Sunitinib as second line (Chi-square test used for the statistical analysis).

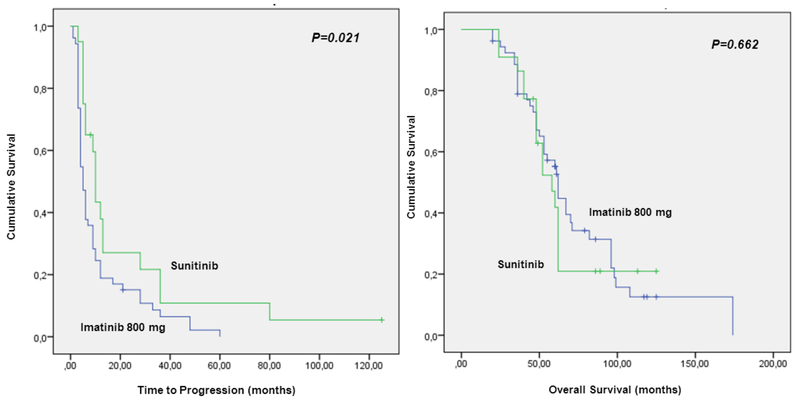
	Number of patients	% of Patients
Secondo line with Sunitinib	44	36%
Second line with Imatinib 800 mg	79	64%
Liver involvment	71	58%
> 2 disease sites	39	32%
Local disease	48	39%
Availabe exact exon 11mutation	94	76%
Deleted exon 11	42	34%

Overall Survival Results

Median follow-up was 61 months.

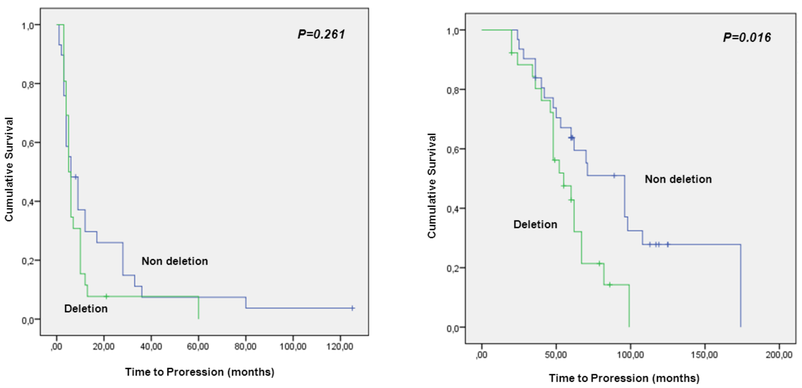
The median time to progression (TTP) in the population treated with sunitinib as a second line treatment was 10 months (95% CI 9.7-10.9) compared with 5 months (95% CI 3.6-6.7) in those who received imatinib 800 mg (P=0.012).

No significant difference was found in term of overall survival (OS) (58 versus 62 months respectively, P=0.883).



Survival according to mutation

Exon 11 cKIT deletion was identified as a prognostic factor in our patients population only for OS (P=0.016), while there was no significant impact on PFS (P=0.261)



Survival and Deletion according to treatment

Time to Progression (months)

TTP	Sunitinb	Imatinib 800 mg/d
Exon 11 Deletion	9 months	6 months
Exon 11 Other Mutations	12 months	24 months
P values	**p 0.683**	**p 0.02**

Overall Survival (months)

OS	Sunitinb	Imatinib 800 mg/d
Exon 11 Deletion	51 months	54months
Exon 11 Other Mutations	58 months	71 months
P values	**p 0.370**	**p 0.063**

Conclusions

In exon 11 mutated GIST patients progressing on a first line treatment with imatinib 400 mg/die, a second line treatment with sunitinib is associated with an improvement in TTP without any impact on survival. Deletion in exon 11 seems to be relevant for sensitivity to imatinib-based therapy as second line in terms of TTP, while the impact of mutation was not identified in patients treated with sunitinib.

The prognostic impact of exon 11 deletion was confirmed in in the whole population only for OS.

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