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Poster No.: RWD158

A Systematic Literature Review of Clinical Practice Guidelines and Real-World Treatment Patterns in Metastatic Gastrointestinal Stromal Tumours in Europe

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BACKGROUND

- Gastrointestinal stromal tumours (GISTs) are the most prevalent malignant mesenchymal tumours in the soft-tissue sarcoma family[1]
- The oncogenic mutations of the genes that encode tyrosine kinase (KIT) and/or platelet-derived growth factor receptor A (PDGFRA) drive over 85% of GISTs[2, 3]
- These are rare tumours with documented incidence ranging from 0.4–2 cases per 100 000 per year.[1] According to the most recent data, the incidence of metastatic GISTs (mGISTs) was eight cases per million[4,5]
- Over the past 20 years, targeted therapies in the form of tyrosine kinase inhibitors targeting KIT, PDGFR and *BCR-ABL* have significantly improved outcomes for patients with GIST[6, 7, 8]

OBJECTIVES

- This systematic literature review (SLR) aimed to identify treatment recommendations based on clinical practice guidelines (CPGs) and to understand real-world patterns of care for mGISTs

METHODS

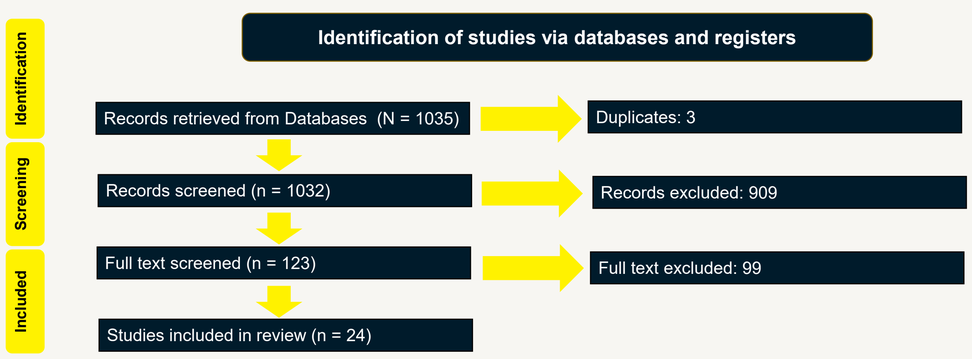
- A systematic literature search of Embase® and MEDLINE® was conducted to identify relevant English-language articles published after 2012 to ascertain CPGs and real-world treatment patterns in patients with mGISTs
- The selection of studies was based on pre-specified inclusion criteria (Figure 1)
- Eligibility of publications was assessed by two independent reviewers, with any discrepancies resolved by a third
- Information regarding line of therapies, treatment patterns, dosage, etc. were extracted from the included studies

Figure 1: Study inclusion criteria

RESULTS

- A total of 1,032 records were screened, 24 of which met the pre-defined inclusion criteria. Eighteen studies reported data for treatment patterns in patients with mGISTs, and six reported CPGs
- The Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram for the SLR is presented in Figure 2

Figure 2: PRISMA flow diagram



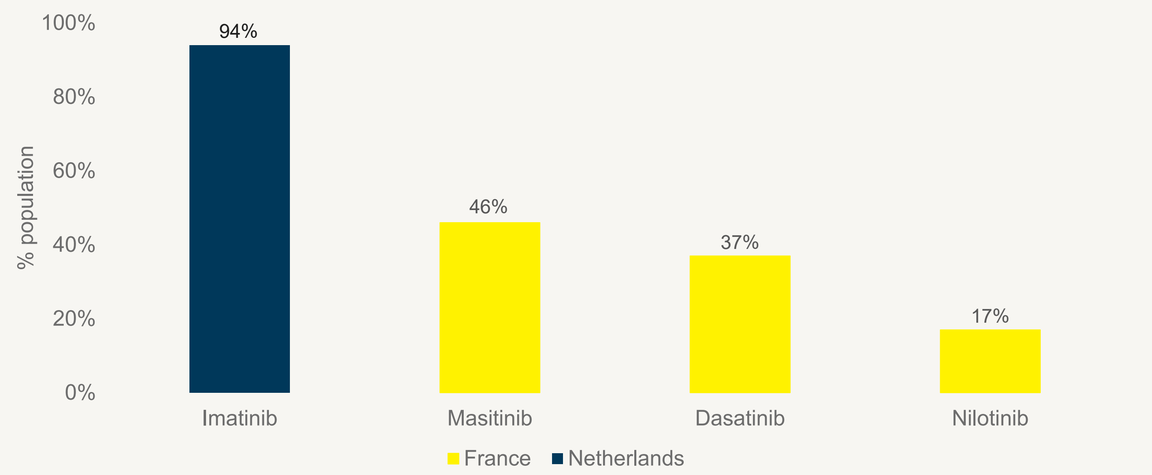
Clinical practice guidelines

- Of the six CPGs identified, two were for Europe as a whole and there was one each for Spain, Germany, the UK and France
- Across all the CPGs, imatinib 400 mg daily is the standard front-line treatment for mGISTs, including for patients who had previously received the drug as adjuvant therapy without relapse during this treatment. Imatinib is also the standard treatment for patients with metastatic disease whose malignancy has been completely removed via surgery
- At a higher daily dose of 800 mg, imatinib is recommended for patients with mGISTs with a *KIT Exon 9* mutation
- European Society for Medical Oncology guidelines recommend avapritinib as a standard treatment for patients with imatinib-non-sensitive mutation
- In the first-line setting, guidelines recommend continuing imatinib indefinitely until disease progression or intolerance. This avoids rapid tumour progression and highlights the importance of patient compliance to therapy
- Following progression to imatinib, the second, third- and fourth-line treatment options are sunitinib (Sutent®) (at a dose of 50 mg daily for 4 weeks on/2 weeks off or, as alternative schedule, 37.5 mg once daily), regorafenib (at the dose of 160 mg daily for 3 out of every 4 weeks) and ripretinib (Qinlock®) (at the dose of 150 mg daily), respectively

Real-world treatment patterns

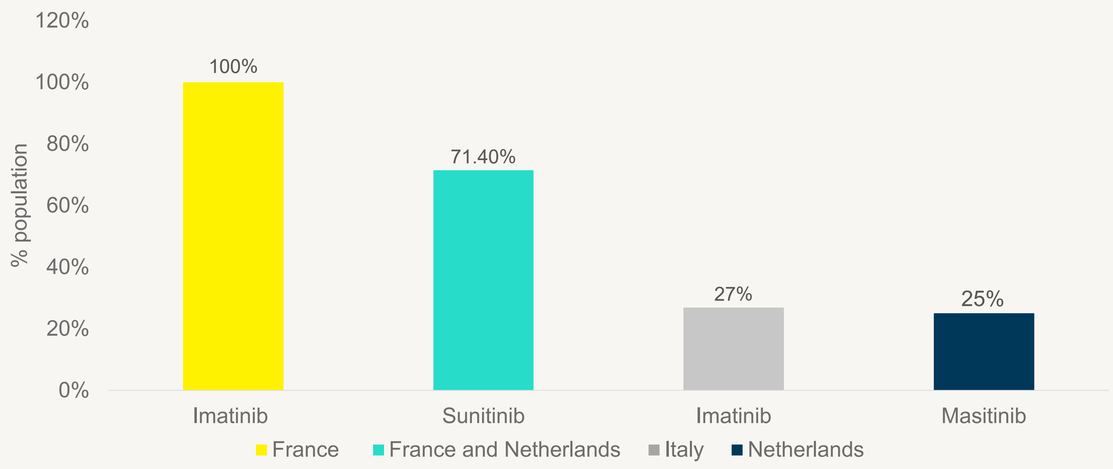
- Of the 18 treatment-pattern studies identified, the reported data were distributed across various countries, including the Netherlands, Germany, France, the UK, Poland, Belgium, Italy, Spain and England
- Real-world treatment patterns also show that imatinib is the first-line treatment of choice in the overall European population (86.1–99.2%)
- Country-specific data for first-line therapy choices are presented in Figure 3

Figure 3: First-line therapy choices



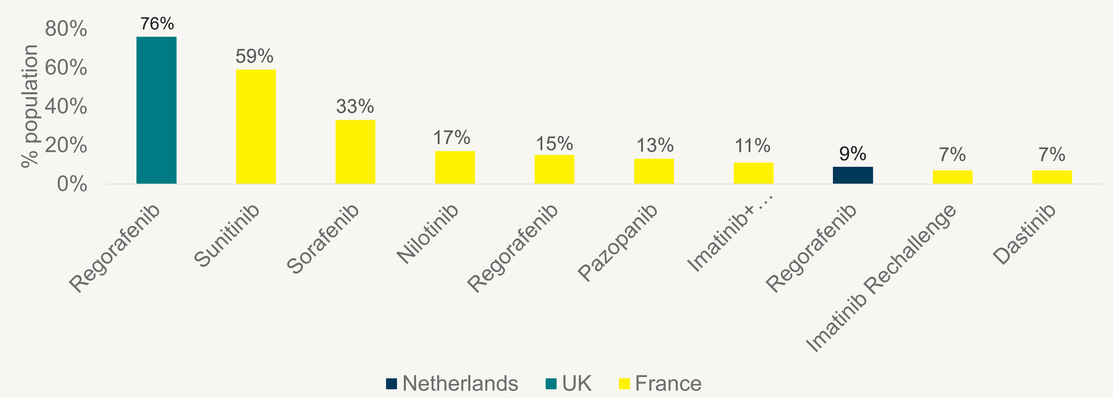
- Strikingly, imatinib was also given as second-line choice (France 100%; Italy 26.8%), as well as third- to sixth-line choice in 9.0–53.0% of patients
- Country-specific data for second-line therapy choices are presented in Figure 4

Figure 4: Second-line therapy choices



- However, for further lines of therapy there is some discord on treatment guidelines, with sunitinib (administered in between 17.6% of patients [France] and 100% [the Netherlands]) and regorafenib (administered in between 10.5% [Netherlands] and 76.0% [UK] of patients) not always being physicians' second- and third-line treatment of choice
- Other therapeutic options for subsequent lines of therapy included avapritinib, cabozantinib and nilotinib (Tasigna®) (Figure 5)

Figure 5: Third- and subsequent-line therapy choices



Limitations

- Most of the results are based on prescription claims, which only indicate the filling of prescriptions, not that they have been taken
- There might be operator error while coding the diagnosis

CONCLUSIONS

- European CPGs recommend imatinib, sunitinib and regorafenib as first-, second- and third-line treatment options for mGISTs, respectively
- There is agreement between first-line therapy recommendations made by CPGs and actual treatment patterns (i.e. imatinib)
- However, in real-world settings, recommendations for subsequent lines are not always adhered to
- We advise prospectively registering patients with GIST in a sizable global database and looking into the use of targeted treatments in patients with metastatic disease

REFERENCES

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An electronic version of the poster can be viewed by scanning the QR code.

Poster presented at the 2022 ISPOR Europe; 06–09 November 2022; Vienna, Austria.