OBJECTIVES
To date, there are no head-to-head comparisons of tyrosine kinase inhibitors (TKIs) regarding treatment flow in chronic myeloid leukaemia (CML). The available evidence is limited to observational studies of small size. This study aims to understand treatment patterns of TKIs and relevant side effects in CML.

METHODS
Data from a large sample of 5,610 CML patients collected from October 2016 to March 2018 across Spain, Italy, Germany, France and UK were analysed. Historic records of patients receiving TKIs (treatment duration, reasons for discontinuation and side effects) were evaluated (n=965). The source of data was a large cross-sectional database of comprehensive patient case information updated on a quarterly basis. Patients included (i) have a current diagnosis of CML; (ii) are currently receiving any drug therapy; (iii) must be the first consecutive cases personally treated by the physician during the reporting period.

RESULTS
➢ Most CML cases reported were receiving a 1st line treatment (84%; n=4,682).
   ✓ 1st generation TKIs are the most used across EUS countries on average (ranging 41% in Germany to 80% in France), followed by 2nd generation (from 20% use in France to 59% use in Germany).
   ✓ In patients in 2nd line treatment (13%; n=750), usage of 2nd generation TKIs across EUS surpassed 1st generation TKIs (~88%).
   ✓ The greatest use of 2nd generation TKIs in 2nd line is observed in the UK with 97%, followed by 90% in Spain.
   2nd generation TKIs also lead the market in 3rd line treatment in most of the European countries assessed (67% - 94%). However in Germany, 3rd generation TKIs were dominant (64%).
   Overall, CML patients in 1st line are likely to receive 1st generation TKIs (77% of historic records) and subsequently move on to 2nd generation TKIs in 2nd line of treatment (88% of current cases).
   The flow between 2nd and 3rd line of treatment shows a majority of patients receiving 2nd generation TKIs in both lines of therapy. However, 33% of the population in 3rd line moved from 2nd generation TKIs to 3rd generation TKIs in their 3rd line treatment.
   The longest average duration of treatment was reported in 1st line (92 weeks), followed by 2nd and 3rd line (74 and 57 weeks respectively).
   "Side effects" was the most common reason for stopping TKI treatment, ranging ~24% in 1st line to ~44% in 3rd line. These ranged ~22% for 1st generation TKIs to ~33% in 2nd and 3rd generation TKIs. Among side effects reported, oedema, nausea, vomiting, diarrhoea, anorexia and rash were the most frequently reported for 1st and 2nd generation TKIs (~5% to ~18%), whilst hepatic dysfunction was the most common for 3rd generation TKIs (43%).

CONCLUSIONS
➢ In EUS countries, 1st generation TKIs are the preferred option in 1st line for most patients; while 2nd generation TKIs lead the market both in 2nd and 3rd lines of treatment.
➢ Differences by line regarding treatment duration and side effects were observed across different generation of TKIs.
➢ An evaluation of the results presented sheds light into TKI-treatment patterns and flow along lines of therapy, which could be used to identify a relevant comparator for economic models or to design other comparative studies in the future.

References
1. Lipson J. Comparative efficacy of tyrosine kinase inhibitor treatments in the first-line setting, for chronic-phase chronic myelogenous leukaemia after failure of second-generation tyrosine kinase inhibitors. Leuk Lymphoma. 2012;53(1):59-64

TKI generations
1st generation: Imatinib  2nd generation: Dasatinib, Sprinzak, nilotinib, bosutinib  3rd generation: Ponatinib

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