1540P **Ripretinib as ≥4th-line treatment in patients with advanced gastrointestinal stromal tumor: Long-term update from the phase III INVICTUS study**

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Background: Ripretinib is an approved switch-control tyrosine kinase inhibitor (TKI) that broadly inhibits mutant KIT and PDGFRA kinase signaling. In INVICTUS, a randomized, double-blind, placebo-controlled trial in ≥4th-line advanced GIST, ripretinib compared with placebo (PBO) significantly improved median progression-free survival (mPFS; 6.3 vs 1.0 months), reducing the risk of disease progression or death by 85%, and showed a clinically meaningful improvement in median overall survival (mOS; 15.1 vs 6.6 months); data as of May 31, 2019 (ESMO 2019). Ripretinib is well tolerated. Here, we present a long-term update of mature data, with a data cut-off date 19 months after the data cut-off date of the primary analysis.

Methods: Patients with advanced GIST previously treated with at least imatinib, sunitinib, and regorafenib were randomized (2:1) to ripretinib 150 mg once daily (QD) or PBO. Upon disease progression determined by blinded independent central review, patients on PBO could cross over to ripretinib 150 mg QD. All patients who received 150 mg QD and had radiological progression could receive 150 mg twice daily.

Results: As of January 15, 2021, of 129 patients randomized, 128 received treatment (ripretinib 150 mg QD, n = 85; PBO, n = 43). Patients randomized to ripretinib had a mPFS of 6.3 months (95% CI 4.6−8.1) vs 1.0 (95% CI 0.9−1.7) month for patients on PBO with a hazard ratio (HR) of 0.16. The mOS in the ripretinib arm was 18.2 months (95% CI 13.1−30.7) vs 6.3 (95% CI 4.1−10.0) months in the PBO arm with a HR of 0.41. No new safety concerns were identified with longer exposure to ripretinib.

Conclusions: Evaluation of primary and secondary endpoints in the phase 3 INVICTUS trial, with a cutoff date 19 months after the primary analysis, demonstrate stable mPFS with no change since the primary data release, and improved mOS for patients randomized to ripretinib. These more mature data continue to support the clinically meaningful benefit in PFS and OS for ripretinib with an acceptable safety profile in patients with advanced GIST treated with 3 or more prior TKIs.

Clinical trial identification: NCT03353753.

Editorial acknowledgement: Editorial writing support was provided by Helen Rodgers, PhD, of AlphaBioCom, LLC, King of Prussia, PA.

Legal entity responsible for the study: Deciphera Pharmaceuticals, LLC.

Funding: Deciphera Pharmaceuticals, LLC.

Disclosure: M. von Mehren: Financial Interests, Personal, Advisory Role: Deciphera; Financial Interests, Personal, Advisory Role: Blueprint; Financial Interests, Personal, Advisory Role: Exelis; Financial Interests, Personal and Institutional, Research Grant: Novartis; Financial Interests, Institutional, Research Grant: Deciphera; Financial Interests, Institutional, Research Grant: Blueprint; Financial Interests, Institutional, Research Grant: Arog; Financial Interests, Institutional, Research Grant: Gradalis; Financial Interests, Institutional, Research Grant: GenMab; Financial Interests, Institutional, Research Grant: ASCO; Financial Interests, Personal, Other, Travel/Accomodations/Expenses: Deciphera; Financial Interests, Personal, Other, Travel/Accomodations/Expenses: NCCN. M.C. 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https://doi.org/10.1016/j.annonc.2021.08.870

1541P Real-world data from patients with gastrointestinal stromal tumors (GIST) treated in Dutch GIST expertise centers

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Background: Introduction of tyrosine kinase inhibitors (TKIs) led to a greatly improved survival of advanced gastrointestinal stromal tumors (GIST). Imatinib was registered as first line palliative therapy in 2001 with a median progression free survival (mPFS) of 20.3 months. Furthermore, sunitinib and regorafenib have shown efficacy in the registration studies (mPFS of 5.6 months and 4.8 months resp.). Still, development of novel agents is needed to overcome TKI resistant GIST. The aim of this retrospective cohort study was to provide real-world response and survival data of approved TKIs to serve as reference point for new agents under development.

Methods: All patients diagnosed with GIST between 2009-2020, treated in 5 expertise centers in the Netherlands were registered in the Dutch GIST Registry and included. The objective response rate (ORR) for patients with advanced GIST treated with imatinib, sunitinib and regorafenib was calculated and subdivided by mutation subgroup. Furthermore, mPFS and overall survival (OS) were estimated using the Kaplan-Meier method.

Results: In total 1253 patients were included, 330 (26%) of them had advanced GIST at diagnosis. Overall, 419 patients were treated with TKIs in the palliative setting. The ORR for imatinib was 62% for all patients, 70% for *KIT* exon 11 mutated GIST, 40% for patients with a *KIT* exon 9 mutation and 48% for the group with other mutations. Patients benefited from imatinib with a mPFS of 34 months (95% confidence interval (CI): 29.8-38.2). Treatment with sunitinib and regorafenib resulted in mPFS of 11 months (95% CI: 8.9-13.1) and 7 months (95% CI: 4.3-9.8) respectively. The median OS for imatinib was 63 months (95% CI: 58.1-67.9), for sunitinib 21 months (95% CI: 15.5-26.5), and for regorafenib 13 months (95% CI: 10.9-15.1).

Conclusions: The response rate and survival outcomes of approved TKIs observed in this cohort demonstrate real-world data on treatment of advanced GIST. Compared to the registration studies, survival in real-life is significantly longer. Therefore, these results can serve as a new reference model for the future phase 3 therapeutic studies for advanced GIST, to compare and set targets for clinical benefit of novel agents.

Legal entity responsible for the study: The authors.

Funding: Dutch GIST Registry was received from Deciphera, Novartis, Pfizer and Bayer.

Disclosure: R.H. Mathijssen: Financial Interests, Personal, Advisory Role, Consulting/advisory role: Servier; Financial Interests, Personal and Institutional, Other, patent: Pamgene (pending); Financial Interests, Institutional, Sponsor/Funding: Astellas; Financial Interests, Institutional, Sponsor/Funding: Bayer; Financial Interests, Institutional, Sponsor/Funding: Boehringer ingelheim; Financial Interests, Institutional, Sponsor/Funding: Cristal therapeutics; Financial Interests, Institutional, Sponsor/Funding: Pamgene; Financial Interests, Institutional, Sponsor/Funding: Pfizer; Financial Interests, Institutional, Sponsor/Funding: Novartis; Financial Interests, Institutional, Sponsor/Funding: Roche; Financial Interests, Institutional, Sponsor/Funding: Servier; Financial Interests, Institutional, Sponsor/Funding: Sanofi; Financial Interests, Personal, Invited Speaker: Novartis. H. Gelderblom: Financial Interests, Institutional, Sponsor/Funding: Novartis; Financial Interests, Institutional, Sponsor/Funding: Ipsen; Financial Interests, Institutional, Sponsor/Funding: Deciphera; Financial Interests, Institutional, Sponsor/Funding: Daiichi Sankyo. N. Steeghs: Financial Interests, Institutional, Advisory Role: Boehringer Ingelheim; Financial Interests, Institutional, Sponsor/Funding: Boehringer Ingelheim; Financial Interests, Institutional, Advisory Role: Ellipses Pharma.; Financial Interests, Institutional, Advisory Role: AIMM Therapeutics; Financial Interests, Institutional, Sponsor/Funding: Astrazenica/medimmune; Financial Interests, Institutional, Sponsor/Funding: bayer; Financial Interests, Institutional, Sponsor/Funding: bristol-Myers Squibb; Financial Interests, Institutional, Sponsor/Funding: Novartis; Financial Interests, Institutional, Sponsor/Funding: GlaxoSmithKline; Financial Interests, Institutional, Sponsor/Funding: Pfizer; Financial Interests, Institutional, Sponsor/Funding: Roche; Financial Interests, Institutional, Sponsor/Funding: Genentech/Roche; Financial Interests, Institutional, Sponsor/Funding: Blueprint Medicines; Financial Interests, Institutional, Sponsor/Funding: AB Science; Financial Interests, Institutional, Sponsor/Funding: Deciphera; Financial Interests, Institutional, Sponsor/Funding: Genentech; Financial Interests, Institutional, Sponsor/Funding: Merck Sharp & Dohme; Financial Interests, Institutional, Sponsor/Funding: Amgen; Financial Interests, Institutional, Sponsor/Funding: Merus; Financial Interests, Institutional, Sponsor/Funding: Lilly; Financial Interests, Institutional, Sponsor/Funding: Incyte; Financial Interests, Institutional, Sponsor/Funding: Pierre Fabre; Financial Interests, Institutional, Sponsor/Funding: Abbvie; Financial Interests, Institutional, Sponsor/Funding: Actuate Therapeutics; Financial Interests, Institutional, Sponsor/Funding: Sanofi; Financial Interests, Institutional, Sponsor/Funding: Cytovation; Financial Interests, Institutional, Sponsor/Funding: InteRNA; Financial Interests, Institutional, Sponsor/Funding: Array BioPharma; Financial Interests, Institutional, Sponsor/Funding: Cantargia AB; Financial Interests, Institutional, Sponsor/Funding: Taiho Pharmaceutical; Financial Interests, Institutional, Sponsor/Funding: Takeda. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.08.871

1542P Kaposi sarcoma: A population-based study of secondary primary neoplasms

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Background: To investigate, in a population-based study, the risk of developing second primary neoplasms (SPNs) after a diagnosis of primary Kaposi sarcoma.

Methods: Data on a cohort of patients with a diagnosis of primary Kaposi sarcoma as their first malignancy were extracted from the Surveillance, Epidemiology, and End Results US registry from 1975 to 2017. Observed-to-expected ratio of developing SPNs was calculated to estimate relative risk (RR) and associated 95% confidence interval (CI), which were compared to a reference population (RP) matched for age, sex, race, and calendar year.

Results: A total of 16,206 patients with primary Kaposi sarcoma were identified, 7.4% of whom developed SPNs (1,199/16,206). Mean age at Kaposi sarcoma diagnosis was 42 years old, while that at SPNs diagnosis was 52. There was a significant risk of SPNs development in Kaposi sarcoma patients compared to the RP ($p < 0.05$). Patients 2 to 11 months after Kaposi sarcoma diagnosis had the highest risk of developing SPNs [RR: 6.9 (95% CI: 6.15—7.8); $p < 0.05$], with Non-Hodgkin Lymphoma as the most common malignancy. Stratification by sex revealed an increased risk of cancer development in males [RR: 2.6 (95% CI: 2.4—2.7); $p < 0.05$]. Patients aged 25-29 years old experienced the greatest burden of SPNs with a significant risk compared to the RP [RR: 13.4 (95% CI: 10.4-17.0) $p < 0.05$].