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INFINITY

A REGISTRY ON DECISION MAKING AND CLINICAL IMPACT OF BIOMARKER-DRIVEN PRECISION ONCOLOGY IN ROUTINE CLINICAL PRACTICE

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BACKGROUND

Treatment decision-making based on molecular alterations instead of defined tumor types is becoming increasingly important in oncology and hematology. Particularly in situations where no standard treatment is available patients are often treated with a targeted therapy matched to a potentially actionable molecular alteration outside of the labelled indication. However, outcome of this treatment approach is not systematically collected, analyzed, and reported.

Results from several clinical trials on precision oncology have suggested improved outcome of matched compared to conventional therapies[1,2]. However, especially real-world data on usage of targeted therapies in a tumor-agnostic approach outside their labelled indications is still scarce. The INFINITY project aims to systematically analyze this treatment approach in routine clinical care.
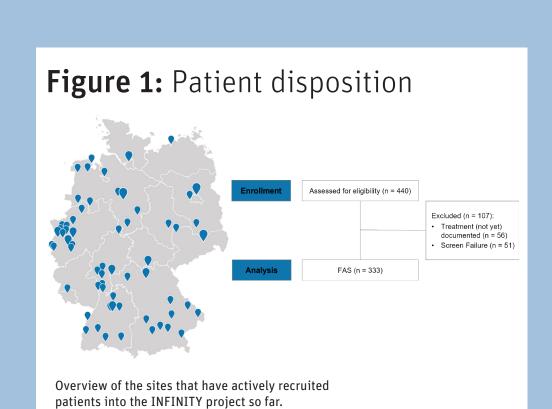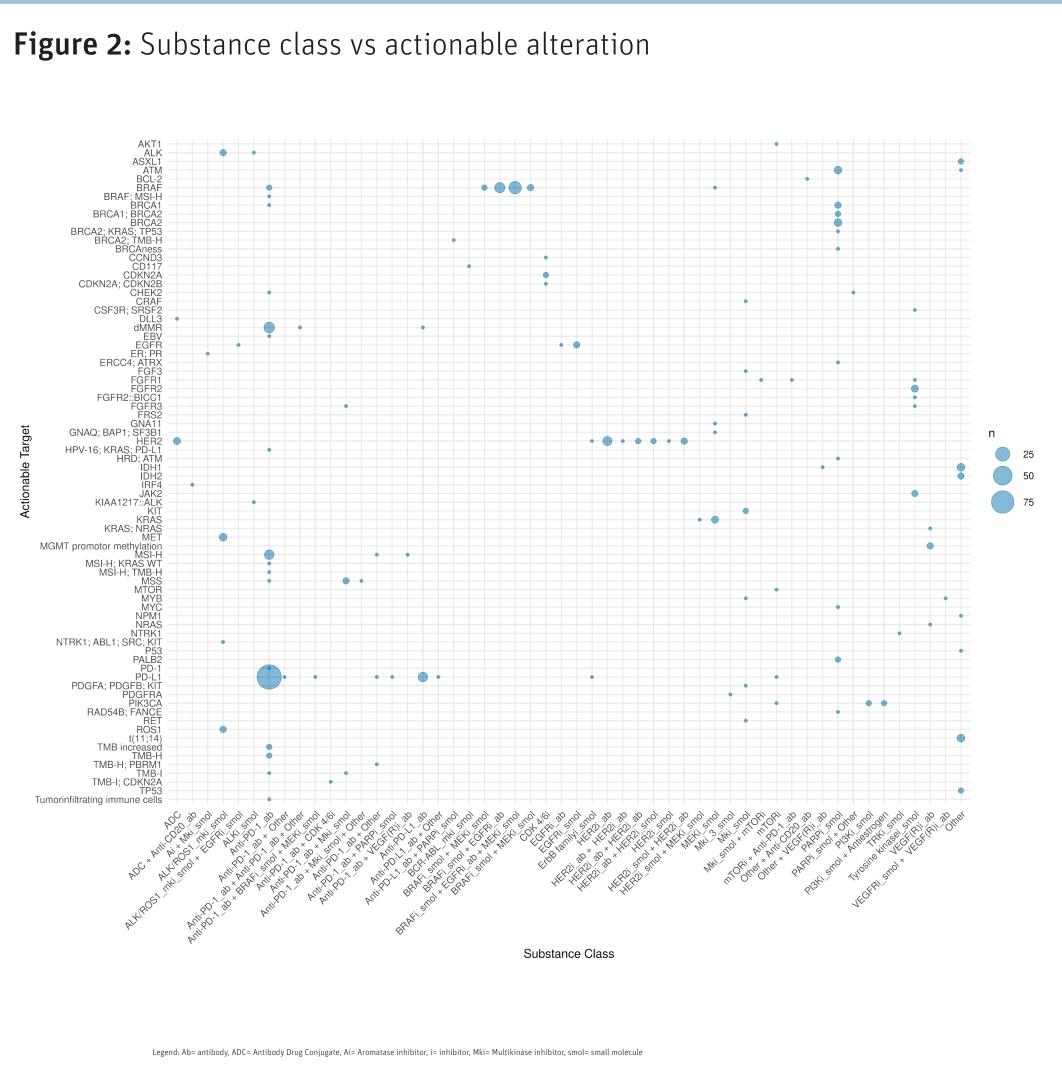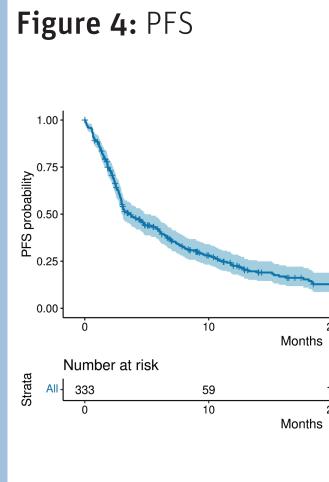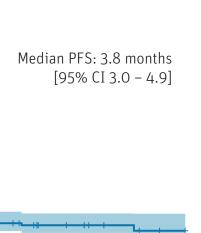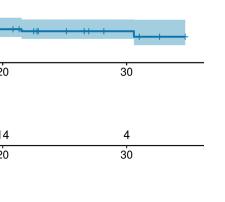
CONCLUSION

INFINITY provides real-world precision oncology data, focusing on specific drug class / alteration matches used outside their approved indications. In this second interim analysis, most common molecular alterations driving targeted therapies included PD-L1 expression, MSI status and BRAF gene alterations. Preliminary outcome results suggest a treatment benefit of molecularly targeted therapies over previous therapy for more than a quarter of patients achieving a PFS ratio ≥1.3. Precision oncology registries are feasible and provide access to real-world data generated by clinics as well as office-based practitioners.
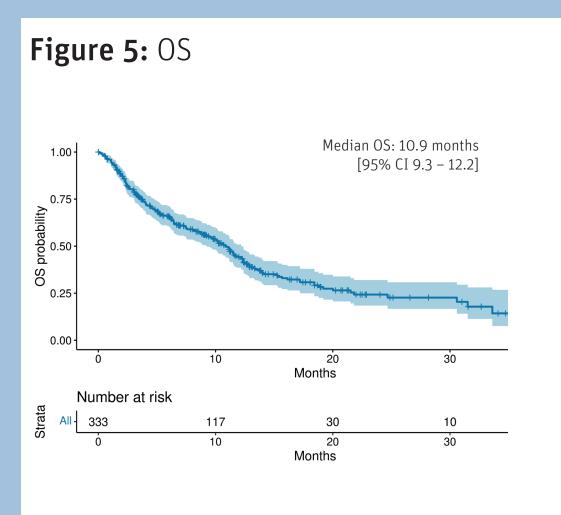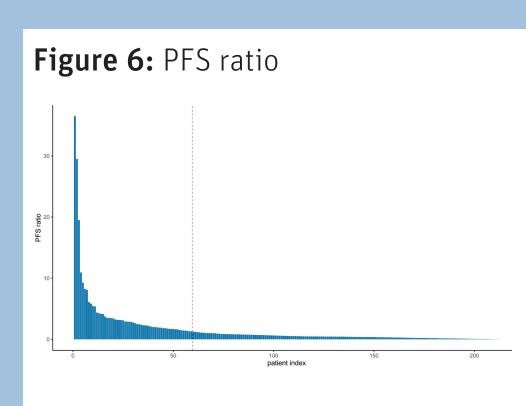
METHODS

INFINITY is a retrospective, observational study conducted at 100 sites in Germany (office-based oncologists/hematologists and hospitals). 500 patients with advanced solid tumors or hematological malignancies not eligible for standard therapy options who received a non-standard targeted therapy (NSTT) based on a potentially actionable molecular alteration will be included. Details on patient and disease characteristics, treatment, outcome, physician's decision-making, and molecular testing will be collected. Furthermore, a decentralized biobank is established. We herein present results from the second interim analysis.

RESULTS

From 30.04.2020 to 30.06.2021, 440 patients were registered at 69 sites. Database cut for this second interim analysis was the 31.10.2021. 333 patients qualified for analysis in the full analysis set (**Figure 1**). Patient characteristics are shown in **Table 1**. Median age was 62.2 years, median time from primary diagnosis to start of first documented NSTT was 22.5 months.

Most patients were treated by office-based (hematologist-)oncologists (n=237, 71.2%). The majority (n=216, 64.9%) had received ≥2 prior therapy lines. Most frequent cancer entities were colorectal (n=66, 19.8%), esophageal (n=22, 6.6%), breast and gastric cancer (n=20, 6.0% each). Most frequently applied NSTT substance classes were PD-(L)1 antibodies (n=157, 47.1%) and BRAF inhibitors (n=35, 10.5%). Accordingly, most frequent actionable biomarkers/alterations which were decisive for the NSTT were PD-L1 status, microsatellite instable (MSI) status and BRAF gene alterations (**Figure 2,3**).

Preliminary progression-free and overall survival (PFS, OS) showed a median PFS of 3.6 months (**Figure 4**) and a median OS of 10.9 months in the total population (**Figure 5**). Median PFS for subgroups was similar, median OS was slightly different (**Table 2**).

For 212 patients, information to calculate the PFS ratio was available. A PFS ratio ≥1.3 was achieved in 27.8% (59/212) of patients in the total population (**Figure 6**), 24.7% (24/97) of patients with PD-(L)1 antibody therapy, and 24.1% (7/29) with BRAF inhibitor therapy.

Figure 1: Patient disposition

Overview of the sites that have actively recruited patients into the INFINITY project so far.

Figure 2: Substance class vs actionable alteration

Figure 3: Entity vs actionable alteration

Legend: Abs= antibody, ADC= Antibody Drug Conjugate, Ai= Aromatase inhibitor, i= inhibitor, Mi= Multikinase inhibitor, pmol= small molecule

Table 1: Patient characteristics (n=333)

Characteristics	N (%)
Sex	
Female	170 (51.1)
Male	163 (48.9)
Age at start of NSTT	
Median, years (min-max)	62.2 (25.8 – 91.5)
<70	248 (74.5)
≥70	85 (25.5)
ECOG Performance Status at start of NSTT	
0	90 (27.0)
1	144 (43.2)
2	60 (18.0)
3	12 (3.6)
4	0
Missing	27 (8.1)
Time since initial diagnosis to start of NSTT	
Median, months (min–max)	22.5 (0.2 – 331.7)
Number of prior systemic therapy lines	
0	32 (9.6)
1	85 (25.5)
2	91 (27.3)
3	59 (17.7)
4	35 (10.5)
≥5	31 (9.3)
Tumor type	
Hematological malignancy	23 (6.9)
Solid tumor	310 (93.1)
Center type	
Hospital	27 (8.1)
Office-based oncologists	237 (71.2)
MVZ (medical care center)	69 (20.7)

NSTT = non-standard targeted therapy

Figure 4: PFS

Median PFS: 3.8 months [95% CI 3.0 – 4.9]

Figure 5: OS

Median OS: 10.9 months [95% CI 9.3 – 12.2]

Table 2: PFS and OS rates in total and subgroups

	Total (n = 333)	Subgroup PD-(L)1-antibody (n = 157)	Subgroup BRAF-inhibitor (n = 35)
Median follow-up since start of NSTT (months)	13.1 [95% CI 12.4 – 16.5]	12.8 [95% CI 12.6 – 19.0]	20.8 [95% CI 12.6 – NA]
Median PFS (months)	3.6 [95% CI 3.0 – 4.9]	3.2 [95% CI 2.9 – 4.8]	3.5 [95% CI 2.5 – 6.7]
6-month PFS rate (%)	41.3 [95% CI 36.1 – 47.3]	38.1 [95% CI 30.9 – 47.1]	44.4 [95% CI 30.5 – 64.8]
12-month PFS rate (%)	22.6 [95% CI 17.9 – 28.5]	23.3 [95% CI 16.6 – 32.8]	10.9 [95% CI 3.9 – 30.8]
Median OS (months)	10.9 [95% CI 9.3 – 12.2]	11.5 [95% CI 9.2 – 15.2]	8.1 [95% CI 4.9 – 14.1]
6-month OS rate (%)	65.9 [95% CI 60.8 – 71.5]	67.3 [95% CI 60.0 – 75.5]	61.4 [95% CI 46.9 – 80.4]
12-month OS rate (%)	44.3 [95% CI 38.5 – 50.9]	47.4 [95% CI 39.0 – 57.7]	40.0 [95% CI 25.8 – 62.0]

Figure 6: PFS ratio

Patients on the left of the vertical dashed line show PFS ratio ≥1.3 and were considered as responders. To quantify the individual patient benefit from the NSTT, the PFS ratio comparing PFS of NSTT (termed PFS2) with PFS of preceding anti-neoplastic therapy (termed PFS1) was calculated. A longer PFS2 compared to PFS1 might be an indicator for effectiveness of the NSTT, thus a higher PFS ratio indicates potentially higher treatment benefit.