FIRST INTERIM ANALYSIS OF INFINITY

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

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Conflicts of interest:

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INTRODUCTION

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 some clinical trials on precision oncology have suggested improved outcome of matched vs. unmatched therapies[1,2]. Recently, first interim results from the non-randomized single-center CATCH program, using whole-genome sequencing and RNA sequencing to guide therapy decisions in the clinical management of metastatic breast cancer patients, were reported[3]. Clinical benefit was achieved in 40% of patients treated according to molecular tumor board recommendation. 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 therapy / alteration matches applied outside of the approved indication of the drug. In this first interim analysis, most common molecular alterations driving targeted therapies included PD-L1 expression, microsatellite status and BRAF gene alterations. Preliminary outcome results suggest a potential benefit (tumor control) in approximately one third of patients. Precision oncology registries are feasible and provide access to real-world data generated by clinics as well as office-based practitioners. Future analyses will also include further endpoints including PFS, PFS ratio and OS.

METHODS

Study design and participants

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 are included.

Data of patients is documented retrospectively four times in annual 3-month intervals. Details on patient and disease characteristics, treatment, outcome, physician's decision-making, and molecular testing will be collected. We herein present results from the first interim analysis.

Interim analysis

Descriptive statistics are used to summarize continuous variables (median, range) and categorical variables (frequencies and proportions). The primary analysis population (full analysis set (FAS)) comprised all patients who fulfilled the in-/exclusion criteria, and for whom start of NSTT has already been documented. In addition, subgroup analyses were performed for the most frequently documented NSTT substance classes: PD-(L)1-directed antibody treatment and BRAF inhibitor treatment. Outcomes included best overall response, overall response rate (ORR, defined as proportion of patients with complete response (CR) or partial response (PR) relative to all patients), and disease control rate (DCR, defined as proportion of patients with CR or PR or stable disease (SD) relative to all patients).

RESULTS

From April 1 to July 31, 2020 209 patients from 41 study sites were registered. 175 patients qualified for analysis in the FAS.

Patient characteristics are shown in **Table 1**. Median age was 60.8 years (29.7-82.7), median time from primary diagnosis to start of first NSTT was 22.2 months (0.8-274.3). The majority of patients (n=122, 69.7%) has received ≥ 2 prior therapy lines. Most of the patients were treated by office-based oncologists (n=125, 71.4%).

Immunohistochemistry (IHC) was the most frequently performed assay to identify actionable alterations (n=99, 56.6% of patients); 50.3% (n=88) of patients received at least one next-generation sequencing (NGS) analysis. For 24.0% (n=42) of cases, discussion at a tumor board has been documented.

Most frequent cancer entities were colorectal (n=44, 25.1%), breast (n=12, 6.9%) and lung cancer (n=10, 5.7%). Most frequently applied NSTT substance classes were PD-(L)1-directed antibodies (n=82, 46.9%) and BRAF inhibitors (n=24, 13.7%). Accordingly, most frequent actionable molecular alterations involved PD-L1 expression, microsatellite instability (MSI) and BRAF gene alterations. **Figure 1** shows the distribution of NSTT substance classes vs. tumor entities, and **Figure 2** the distribution of molecular alterations vs. tumor entities.

Preliminary overall response rate (ORR) in the total population was 17.7% and disease control rate (DCR) was 33.7% (**Table 2**). For patients with PD-(L)1-directed antibody therapy respective ORR was 20.7% and DCR was 34.1%. For patients with a BRAF inhibitor therapy, ORR and DCR were 16.7% and 29.2%, respectively.

Table 1

	Total (n=175)
Sex	
Female	89 (50.9%)
Male	86 (49.1%)
Age at start of NSTT (years), median (min-max)	**60.8 (29.7-82.7)**
<70	135 (77.1%)
≥70	40 (22.9%)
ECOG Performance Status at baseline	
0-1	128 (73.1%)
2	30 (17.1%)
3	5 (2.9%)
Missing	12 (6.9%)
Time from primary diagnosis to start of NSTT (months), median (min-max)	**22.2 (0.8-274.3)**
Number of prior systemic therapy lines	
0	14 (8.0%)
1	39 (22.3%)
2	51 (29.1%)
3	34 (19.4%)
4	21 (12.0%)
≥5	16 (9.1%)
Tumor type	
Hematological malignancy	10 (5.7%)
Solid tumor	165 (94.3%)
Center type	
Hospital	14 (8.0%)
Office-based oncologists	125 (71.4%)
MVZ (medical care centre)	36 (20.6%)

Table 1: Patient characteristics.

NSTT = non-standard targeted therapy

Table 2

	Total (n=175) [95% CI]
Best overall response	
Complete response (CR)	4 (2.3%)
Partial response (PR)	27 (15.4%)
Stable disease (SD)	22 (12.6%)
Stable disease (SD)/No response	2 (1.1%)
Non-progressive disease (Non-PD)	4 (2.3%)
Progressive disease (PD)	67 (38.3%)
Not evaluable	5 (2.9%)
Missing	44 (25.1%)
Overall response rate	**31 (17.7%) [12.7, 24.1]**
Disease control rate	**59 (33.7%) [27.1, 41.0]**

Table 2: Preliminary tumor response to non-standard targeted therapy

Response status as reported by the documenting site during routine care. Patients still under treatment, for whom no response assessment is yet available, are categorized as missing. Furthermore, best response may not have been achieved yet in patients still under treatment. Therefore, estimates on response rates can still change in upcoming analysis.

Figure 1

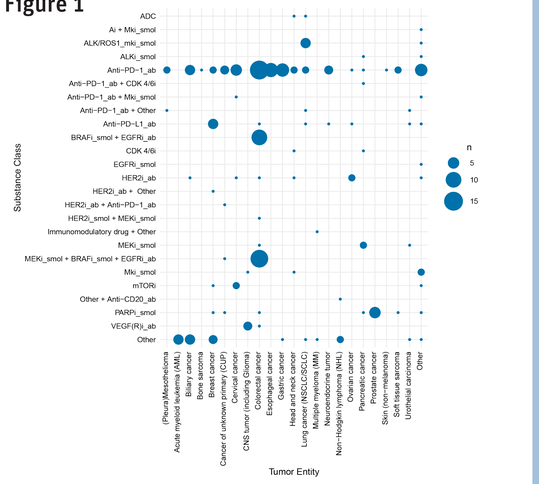

Figure 1: Association between tumor type and NSTT substance class.

139 patients received single agent targeted therapies and 36 received combination targeted therapies. **Abbreviations:** ab = anti-body | ADC = anti-body drug conjugate | Ai = aromatase inhibitor | i = inhibitor | Mki = multi-kinase inhibitor | smol = small molecule

Figure 2

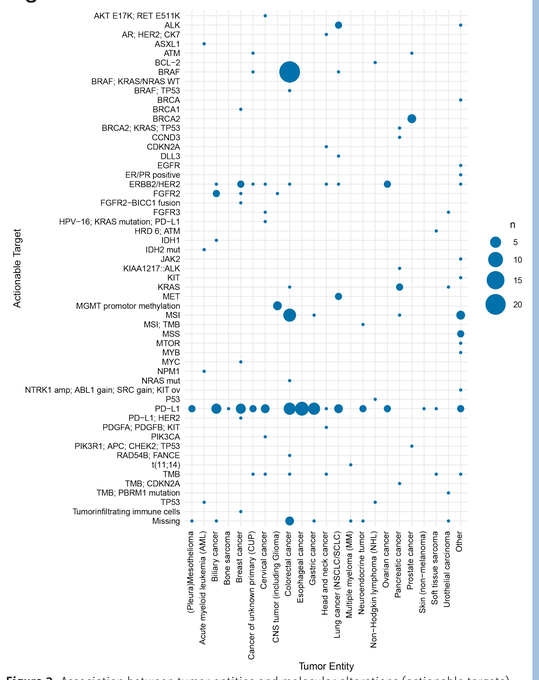

Figure 2: Association between tumor entities and molecular alterations (actionable targets).