The IMPRESS-Norway trial: Improving Public Cancer Care by Implementing Precision Cancer Medicine in Norway

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Background

There is a high demand for precision cancer treatment. Methods for advanced molecular diagnostics are available, and a considerable number of drugs are already approved on specific indications. However, these drugs are only to be used within subgroups of patients with the specific diagnostics determined by clinical studies. Some drugs targeting a specific pathway or gene aberration might just as well be efficient in patients with other tumour types, not yet tested.

Methods

IMPRESS-Norway is national, investigator-initiated, prospective, open-label, non-randomized, combined basket- and umbrella-trial, patients are enrolled into multiple parallel treatment cohorts. Patients with progressive disease with no further standard therapy are eligible. Each cohort is defined by the patient's tumour type, molecular profile of the tumour, and study drug. Currently, 17 drugs are provided by five different pharmaceutical companies or research grants. All drugs available in IMPRESS-Norway are regulatory approved. Treatment outcome in each cohort is monitored by using a Simon two-stage-like 'admissible' monitoring plan to identify evidence of clinical activity. Molecular diagnostics with the TruSight Oncology 500 gene panel (TSO 500) are funded by the public health care system and used for screening. In addition, patients are screened with circulating tumor DNA (ctDNA) analyses. All screened patients are discussed at national molecular tumor board.

Study objectives

The primary objective is to access clinical benefit at 16 weeks of treatment (W16) defined as complete response, partial response or stable disease by RECIST criteria. Secondary objectives include progression free survival, overall survival, patient reported outcomes and other exploratory objectives ie. comparison of ctDNA and tumor DNA analysis, investigation of resistance mechanisms etc.

Results

Patient inclusion

The trial opened for accrual in April 2021. By august 2022, 472 patients have been included in the molecular screening and 428 have completed evaluation in the national molecular tumour board. Based on molecular findings 24% of the patients were included in treatment cohorts in IMPRESS-Norway, 2% in other clinical studies and 10% in different early access programs. 64% of the patients did not have any actionable molecular findings or the potential drugs were not available (Figure 1).

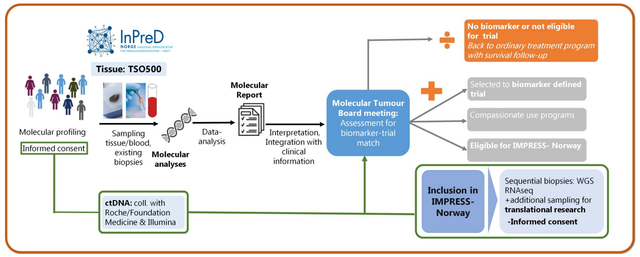


Figure 1. Patient inclusion flow-chart

Tumor types

Over 50 different tumor types were analysed by TSO 500 and ctDNA analysis. Patients with rare tumor types and few treatment options were prioritized. However, most common tumor types like colorectal, breast and lung cancer we were also included and offered molecular profiling (Figure 2).

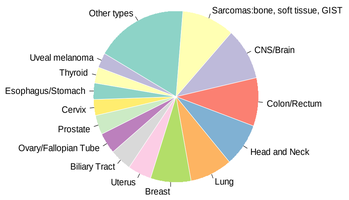
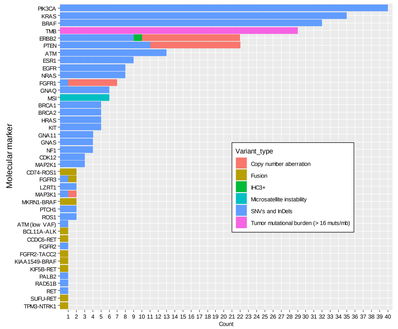


Figure 2. Tumour types analysed in the molecular screening phase (n=328)

Biomarker overview



Alterations in PI3K/AKT/mTOR and RAS/MAPK pathways, changes in ERBB2, FGFR, HRR genes and high tumor mutational burden (TMB) were most commonly detected biomarkers (Figure 3).

Figure 3. Molecular biomarkers identified during screening phase (n=328)

Treatment cohorts

Based on molecular findings, tumor type and available drugs 101 patients were allocated to treatment to currently 70 opened cohorts, and 67 patients have started treatment in IMPRESS-Norway study (Table 1).

Drug	Biomarker	N included	N started treatment
Alectinib	ALK fusion	1	1
Alpelisib	PIK3CA mut	5	3
Alpelisib + Fulvestrant	PIK3CA mut	1	0
Atezolizumab	HML >=16 <=140	13	12
	MSI-high	8	7
	HML > 140 <= 290	1	1
	HML > 290 <= 450	1	1
Imatinib	c-KIT mut	1	0
Pertuzumab + Trastuzumab	ERBB2 mut	8	5
	ERBB2 amp	8	5
	HER2 exp	1	0
Trametinib	GNAQ mut	6	2
	NRAS mut	4	2
	HRAS mut	2	1
	NF1 mut	2	2
	MAP3K1 loss	1	1
	BRAF fusion	1	0
	GNA11 mut	1	0
	MAP2K4 loss/mut	1	0
	LZTR1 loss/mut	1	0
Trametinib + Dabrafenib	BRAF Non-V600 mut	9	6
	BRAF V600E mut	5	5
Vemurafenib + Cobimetinib	BRAF V600E mut	15	10
Vismodegib	SHH-pathway mut	5	3

Table 1. Overview of used drugs, biomarkers and included patients

Treatment results

Early aggregated data show clinical benefit in 50% of the patients at treatment in W16 (26/50). One patient experienced complete response, 6 of 50 patients experienced partial response and 19 stable disease at W16. Treatment was discontinued in 24 patients, 17 due to disease progression or death, and in 7 patients due to adverse effects (Figure 4). Seventeen patients had less than sixteen week on treatment.

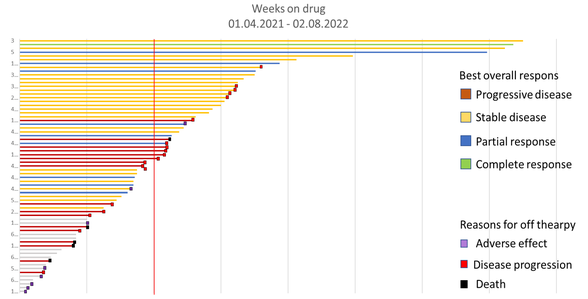


Figure 4. Early aggregated results

Conclusion

Molecular testing is becoming a standard-of-care for all cancer patients in Norway and increasing number of patients now have access to IMPRESS-Norway and other clinical trials. Early data show that a significant number of patients have clinical benefit of treatment received in IMPRESS trial. We plan to continue inclusion over the upcoming years and expand positive cohorts. New drugs and new technologies will be progressively included in the trial.

Funding and Disclosures

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- First author has following financial interests to declare: Have participated in advisory boards and meetigs with Roche, AstraZeneca, Eli Lilly, AbbVie, MSD, BMS, Takeda, Pfizer, Bayer, Janssen. Payments allocated to hospital.