Implementation of Liquid Biopsies during Routine Clinical Care in Patients with advanced Solid Cancer (LIQPLAT) – A Single Arm Trial that enables Randomized Comparisons

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Background

- Genomic heterogeneity and consecutive treatment resistance poses one of the major challenges in the management of solid cancers
- In solid cancers, the molecular pattern derived from a single biopsy is often limited to a single anatomical site and a specific point in time
- In contrast to this, liquid biopsies, especially circulating tumor DNA (ctDNA), have the great potential to catch the entire tumor's 'genomic pool'
- Measuring ctDNA has been proposed as a potential tool to advance cancer care by
  i. Identification of targetable alterations
  ii. Assessment of disease burden and treatment response
  iii. Early identification of resistance mutations
  iv. Estimation of patient prognosis and outcomes

- To date, there is little evidence from randomized trials on the implementation of ctDNA measurements, especially in patients with advanced solid cancers

Objective & Eligibility criteria

The primary objective of this trial is to assess the implementation and feasibility of repeated ctDNA measurements during routine clinical care of patients with solid cancers

<u>Feasibility outcomes</u>
- Detectability of ctDNA
- Identification of actionable alterations
- Analysis turnaround time

<u>Clinical outcomes</u>
- Patient-reported quality of life
- Progression-free survival and overall survival
- Time to next treatment line

<u>Key eligibility criteria</u>
- Provided general research consent
- Advanced, not resectable solid malignancy
- Indication for systemic anti-cancer treatment
- No primary brain tumour
- No prior systemic treatment for advanced disease

Study Design

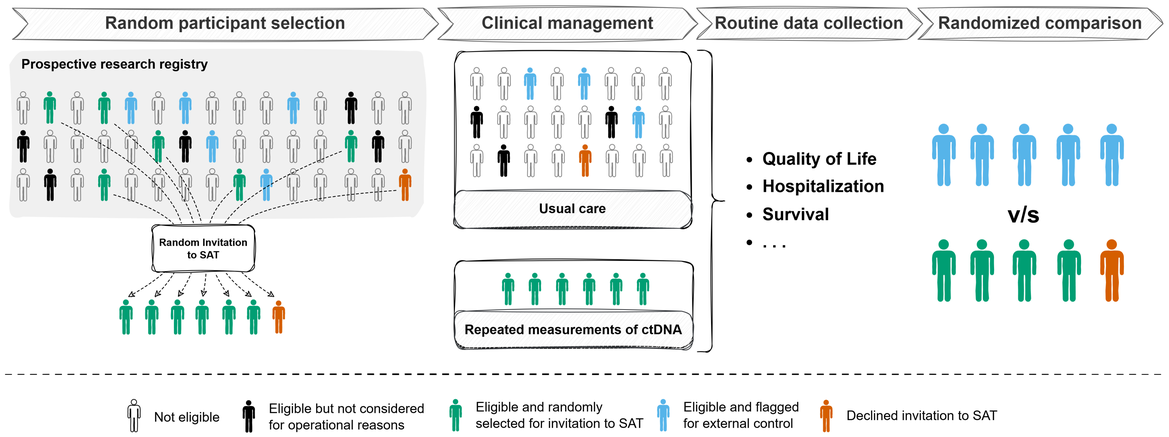

Figure 1. Trial design. Abbreviation: SAT, single-arm trial.

- LIQPLAT is a single arm trial embedded in a prospective research registry at the University Hospital of Basel (Figure 1)
- Eligible patients are randomly selected from a prospective research registry and invited to participate in the trial.
- In parallel, eligible patients from the same cohort are randomly selected and flagged for an external control. Those patients are not offered participation in the trial.
- For all patients, details regarding the tumor entity, treatment, patient outcome (e.g., PFS and OS), and quality of life are collected. For this purpose, the trial almost exclusively uses routinely collected data.
- We aim to include 200 randomly invited patients to receive ctDNA measurements alongside standard care
- The trial is registered at clinicaltrials.gov (NCT06367751) and kofam.ch (SNCTP000005844), (BASEC 2024-00358)

Intervention

All patients receive routine care disease assessment and treatment, <u>plus ctDNA measurement</u>:

1. Before start of medical anticancer treatment.
2. Between the 2nd and 3rd months after treatment start; typically, after a first treatment block.
3. Between the 5th and 6th month of treatment.
4. At any event of suspected or confirmed clinical or radiological disease progression or treatment discontinuation for any reason.

Results are evaluated by a molecular tumor board to guide clinical management.

Patients

- As of October 1st, 162 patients have been selected for invitation
  - Participation was offered to 140 (86%) patients
  - Participation was accepted by 133 (82%) patients
- Patients had a median age of 71 years (IQR 35,89)
- 43 (27%) were female
- 111 (69%) had a performance status of EOCG 0-1
- Lung (40, 25%), head and neck (23, 14%), and colorectal (22, 14%) were most common cancers

Liquid biopsies

- Median turnaround time was 17 days
- At least one Mutation was identified in 85 of 133 (64%) baseline samples
- Most frequent mutations were: TP53 (48, 36%), Kras (22, 17%) and PIK3CA (12, 9%)
- At least one mutation was identified substantially more often in liquid biopsies of patients with adenocarcinoma (75%, 95%CI 66–85) than in those with other histologies (55%, 95%CI 43–67), p = 0.005 (Figure 2).

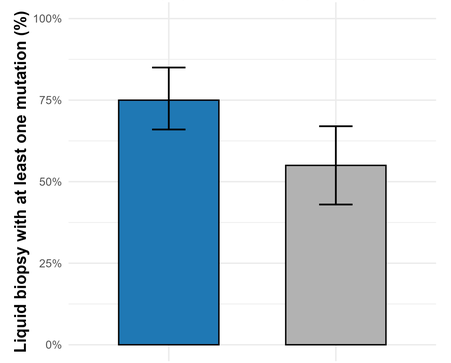

Figure 2. Frequency of liquid biopsies with at least one mutation detec

Conclusion

- The LIQPLAT Trial demonstrates that routine ctDNA measurement is feasible in a real-world cancer population
- The trial's innovative design optimizes resource use, and allows for secondary comparative effectiveness analysis with non-invited patients of the research registry
- Tumor-specific features, (e.g. histology), may influence ctDNA release and consequently impact its clinical applicability in patient management. The influence of tumor-related features (e.g., histology, tumor volume, disease site) and patient characteristics (e.g., age, sex, renal function, inflammatory status) on the probability of ctDNA detection will be evaluated throughout the project.
- Ultimately, LIQPLAT seeks to lay the groundwork for larger trials, possibly paving the way for broader implementation of personalized cancer care based on ctDNA insights.
- Current information is available via liqplat.com

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