Background: The Rome Trial is a randomized phase II trial (NCT04591431). The aim is to evaluate the feasibility on largescale and the clinical utility of a tailored treatment (TT) in patients (pts) compared to standard of care (SoC) with solid tumors. Here we report the preliminary results of the molecular alterations detected during the screening phase.

Results: From Oct 2020 to Apr 2022, 792 pts were enrolled from 40 Italian hospitals. To date, we have complete mutational data of 482 patients. Molecular profiling was available both on tissue and liquid biopsy in 414 (86%) pts, while 13 and 53 had only tissue or liquid test available. 3138 genomic alterations were identified in 258 genes with a median of 7.9 alterations (0-35). The most frequent altered genes were: TP53 (57%), PIK3CA(21%), KRAS (28%), DNMT3A (22%), CDKN2A (19%), APC (16%), PTEN (12%), ARID1A (12%), ERBB2 (11%),NRAS (11%), ATM (10%), TET2 (11%). The most frequent altered pathways were TP53 (57%), RAS/RAF (47%),Cell cycle/cycline (38%), PI3KCA/AKT/MTOR (28%), Homologous Recombination system (20%). The most common actionable alterations with TT available in the ROME trial were: PIK3CA/AKT (24%), H-TMB/MSI (17%), FGFR1/2/3 (9%), EGFR (9%), BRAF V600/nonV600 (6%), JAK 1/2/3 (3%), NTRK1-3/ROS1 (2%), RET (2%), PTCH1(1.5%), ALK (1%).17 pts were MSI (3.5%). Overall median TMB was 9.7 (0-458) while median TMB for MSS and MSI pts were 5.9 (0-35) and 96.0 (24-458), respectively. MSS pts with a TMB >10 mut/mb were 65 (13.5%). Actionable mutations were detected in 202 pts (42%) and 130 (27%) were randomized in the trial after the MTB discussion.

Methods: Centralized NGS was performed on both tumor tissue, collected within 6 months, and liquid biopsy from pts with refractory malignancies. Molecular alterations were evaluated by Molecular Tumor Board (MTB) using COSMIC, ClinVar, OncoKB and VarSome datasets. All pts with actionable genomic alterations were weekly discussed by the MTB. Genes with at least 10% frequency of mutation, microsatellite status (MS) and tumor mutational burden (TMB) were collected.

Study Design:

- **Screening Phase**
  - At least 1280 advanced/metastatic cancer PTS screened
  - Actionable mutation not previously identified with standard Dx = Out of protocol and SoC
  - Molecular Profiling with Foundation One on biopsy and with Foundation ACT on blood
  - Gene expression profile with Nanostring IO360 panel and Nanostring PanCancer Immune panel

- **Identification of Molecular target**
  - TMB/MSI
  - Target therapy according to mutational status

- **Progression of Disease**
  - Molecular Profiling on blood with Foundation ACT
  - Target therapy according to mutational status

- **Randomization 1:1**
  - Investigator choice therapy = SoC
  - Investigator choice therapy = SoC

- **Enrollment data**
  - MSS <10 mut/mb 12.5%
  - MSS >10 mut/mb 75%
  - MSS <10 mut/mb 75%
  - MSS >10 mut/mb 75%
  - MSS <10 mut/mb 75%
  - MSS >10 mut/mb 75%
  - MSS <10 mut/mb 75%
  - MSS >10 mut/mb 75%
  - MSS <10 mut/mb 75%

Conclusion: ROME trial demonstrates the feasibility of extensive molecular profiling and discussion in MTB. Almost 30% of pts had molecular alterations for which a target strategy was available in the trial.