FEASIBILITY AND POTENTIAL IMPACT ON CLINICAL DECISION MAKING OF NGS-BASED GENOMIC PROFILING IN ADVANCED PANCREATIC ADENOCARCINOMA (aPDAC)

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M. Milella[1], V. Vaccaro[1], B. Casini[1], E. Gallo[1], D. Assisi[1], G. Pizzi[1], G. Vallati[1], L.R. Grillo[2], B. Antoniani[1], V. Barucca[3], C. Spoto[4], M. Imperatori[5], G. Grazi[1], E. Pescarmona[1], F. Marandino[1], M.G. Diodoro[1], F. Cognetti[1], S. Buglioni[1]

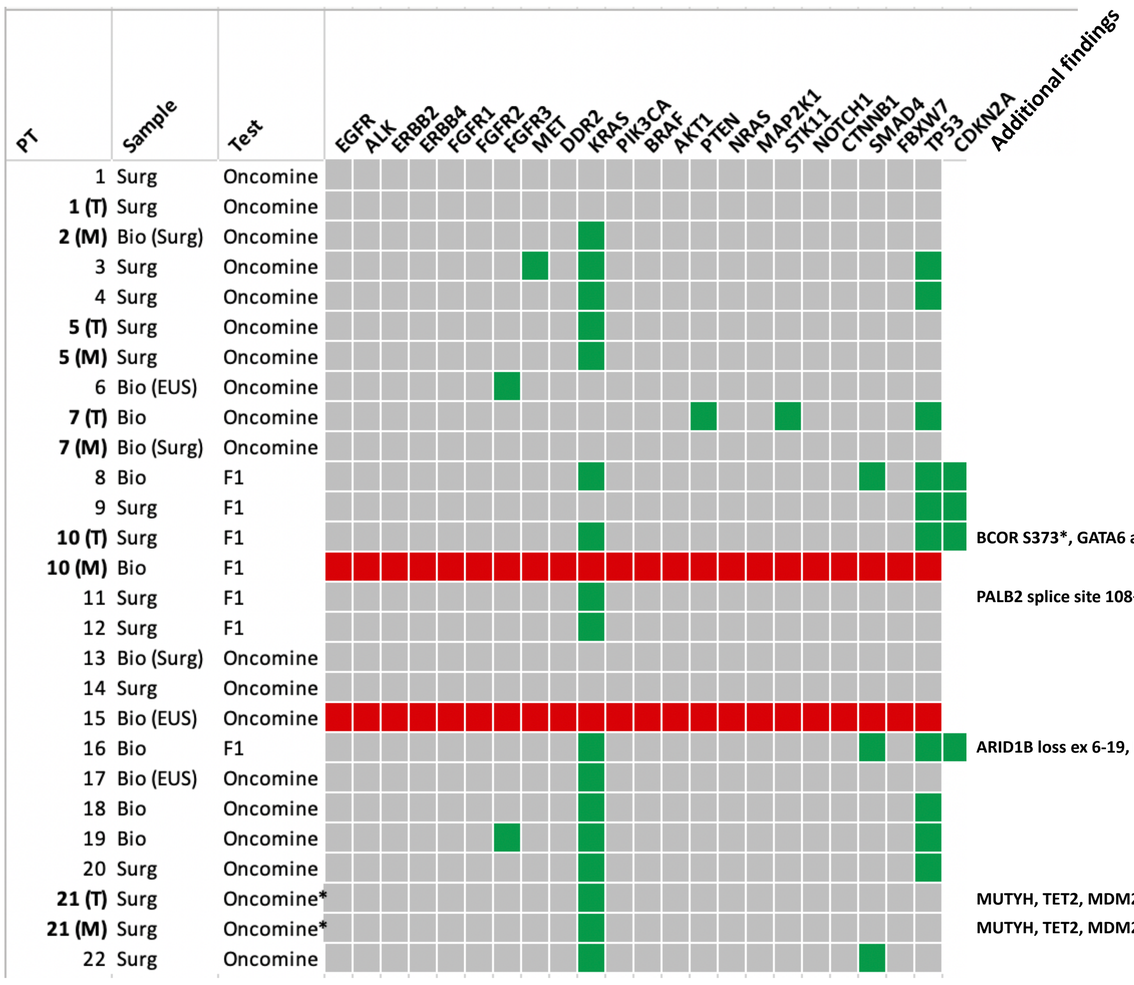
[1]***IRCCS Istituto Nazionale Tumori Regina Elena, Rome***; [2]Azienda Ospedaliera S. Camillo Forlanini, Rome; [3]Ospedale Misericordia, Grosseto; [4]Ospedale S. Maria Goretti, Latina; [5]IRCCS CROB, Rionero In Vulture

Rationale/Background

- Feasibility and potential clinical impact of ***NGS-based genomic profiling*** in aPDAC has not been explored
- ***Tissue procurement*** in advanced disease is perceived as potentially ***problematic***
- No targeted or immunological agents have proven effective so far in aPDAC, calling into question the potential ***clinical relevance*** of molecular profiling in this disease
- Systematic profiling of unselected advanced patients might prove ***unreasonably expensive***, with little clinical impact

Methodological approach

- ***Clinical triggers*** of NGS testing were:
  - ***unusual clinical history***/response to treatment
  - clinical evidence of ***low metastatic potential***
  - ***differential diagnosis*** in metastatic disease
- 27 tests performed in ***22 pts***
- ***Paired T/M*** samples tested in ***5 pts***
- NGS panels employed:
  - ***Oncomine™*** 22-gene panel: 20 pts
  - ***FoundationOne™*** 315-gene panel: 7 pts



Results/1

- Specimen source:
  - ***Surgery*** with radical intent: 15 samples
  - Surgical ***biopsy***: 3 samples
  - ***US or CT-guided*** percutaneous biopsy: 6 samples
  - ***EUS-guided*** biopsy: 3 samples
- ***Failed*** molecular testing: 2 samples
- Panels used:
  - ***FoundationOne™***: 7 samples (1 failed)
  - ***Oncomine™***: 20 samples (1 failed)

Results/2

- No mutations detected: ***5/25***
- KRAS-wt: ***8/25***
- KRAS-mut: ***17/25***
  - ***KRAS only***: 8
  - ***KRAS/TP53***: 8
  - ***KRAS/TP53/CDKN2A***: 4
  - ***KRAS/TP53/SMAD4***: 2
  - ***KRAS/SMAD4***: 1
  - ***TP53 only***: 2
- Additional mutations identified:
  - ***FGFR3*** (F384L, ***2 pts***) – potentially actionable
  - ***MET*** (Ex14 skip) – potentially actionable
  - ***PTEN/STK11*** (TP53, no KRAS) – potentially actionable
  - ***PALB2*** – potentially actionable
  - ***HER-2 ampl*** (ratio 2) – potentially actionable
- Other alterations
  - ***MSS***: 5/5 samples tested
  - ***TMB***: Low in 5/5 samples tested (0-5.5 muts/MB)

Results/3

- ***Paired T/M samples*** analyzed in 5 pts:
  - 1 pt not evaluable (biopsy sample at relapse failed testing)
  - Fully concordant results in 2 pts
  - KRAS-mut in M, but not in T, in 1 pt (***sensitivity issues?***)
  - 1 pt had completely different profiles:
    - ***T: TP53/PTEN/STK11***
    - ***M: no detectable mutations***

  A tentative diagnosis of a ***second NSCLC primary*** was made in this pt and she was treated accordingly.
- Absence of ***SMAD4*** alterations was taken into account to indicate locoregional treatment in 3 pts:
  - ***RT*** to local relapse in 2 pts, following very good PR to CHT
  - ***Liver met surgery*** in 1 pt, following very good PR to I and II-line CHT

Conclusions

- Genomic profiling using targeted NGS panels is ***feasible*** in aPDAC
- "Technical" failures are rare
- Specimens derived from ***percutaneous/EUS-guided FNA(B)*** are suitable for molecular testing
- ***Potentially actionable mutations*** can be found in 1 out of 4/5 pts tested
- Test results may influence ***treatment decisions*** in an additional proportion of patients (differential diagnosis; indication for loco-regional treatment)