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Prognostic significance of metabolomics clusters in extra-pancreatic NETs: Lung NET sub-analysis

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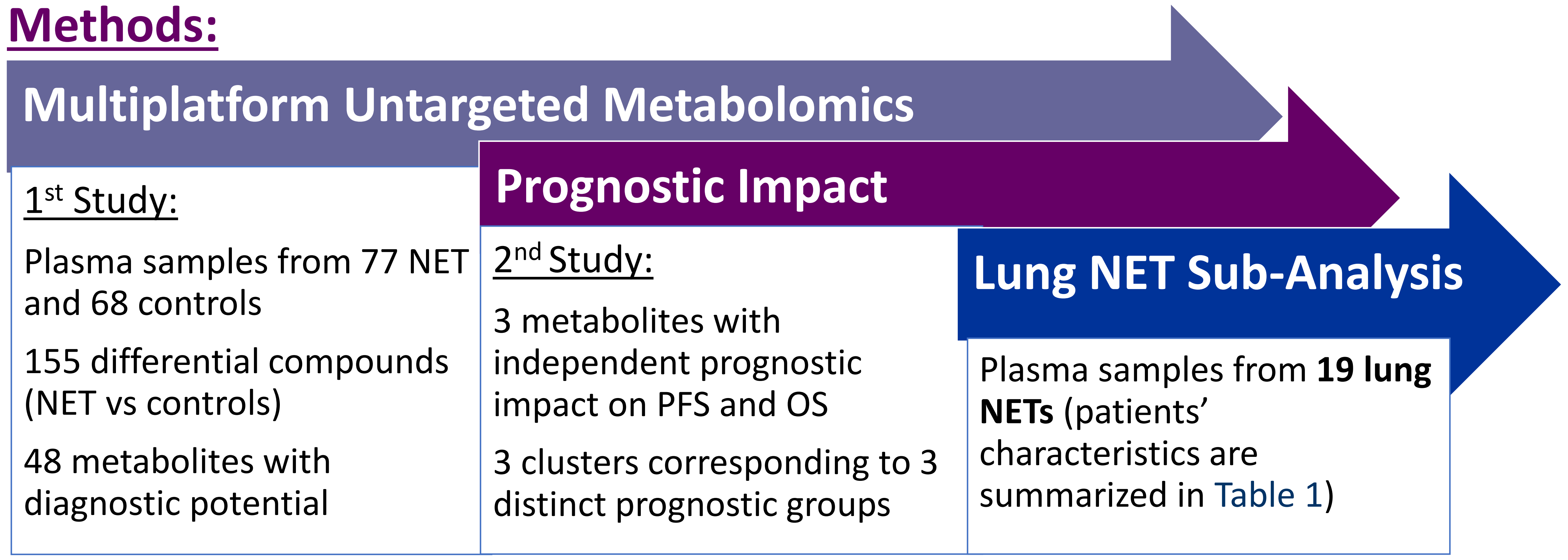
Background:

- ✓ **Metabolic flexibility** is one of the key hallmarks of cancer and metabolites are the final products of this adaptation, reflecting the aberrant changes that support cancer cells proliferation and survival.
- ✓ Previous studies carried out by our group, using a **multiplatform untargeted metabolomic** approach (GC-MS, CE-MS and LC-MS) of plasma samples from 77 extra-pancreatic NET and 68 controls demonstrated that **NET** have a distinctive metabolomic profile [1,2].
- ✓ A 3-metabolite signature was able to stratify patients in **3 distinct prognostic clusters** (numbered as 1, 2 and 3), with cluster 3 associated with the best prognosis.
- ➢ **Aim:** to confirm the prognostic significance of this metabolomic signature in the **NET lung cohort.**

References

1. Soldevilla B, et al. Cancers (Basel). 2021 May 27; 13(11): 2634. doi: 10.3390/cancers13112634.
2. La Salvia A, et al. Eur J Endocrinol. 2024 Jan 3;190(1):62-74. doi: 10.1093/ejendo/lvad160.

Methods:



Multiplatform Untargeted Metabolomics

1st Study:

Plasma samples from 77 NET and 68 controls

155 differential compounds (NET vs controls)

48 metabolites with diagnostic potential

Prognostic Impact

2nd Study:

3 metabolites with independent prognostic impact on PFS and OS

3 clusters corresponding to 3 distinct prognostic groups

Lung NET Sub-Analysis

Plasma samples from **19 lung NETs** (patients' characteristics are summarized in Table 1)

Results:

- ✓ **Cluster 3** was associated with **improved prognosis**, with OS rates at 5 years of 61.9% vs 40% for cluster 3 vs 1 (Figure 1).
- ✓ Multivariate analysis confirmed the **metabolite clusters** to be associated with OS (p=0.067) (Table 2).

Figure 1. Prognostic impact of metabolomics clusters on OS

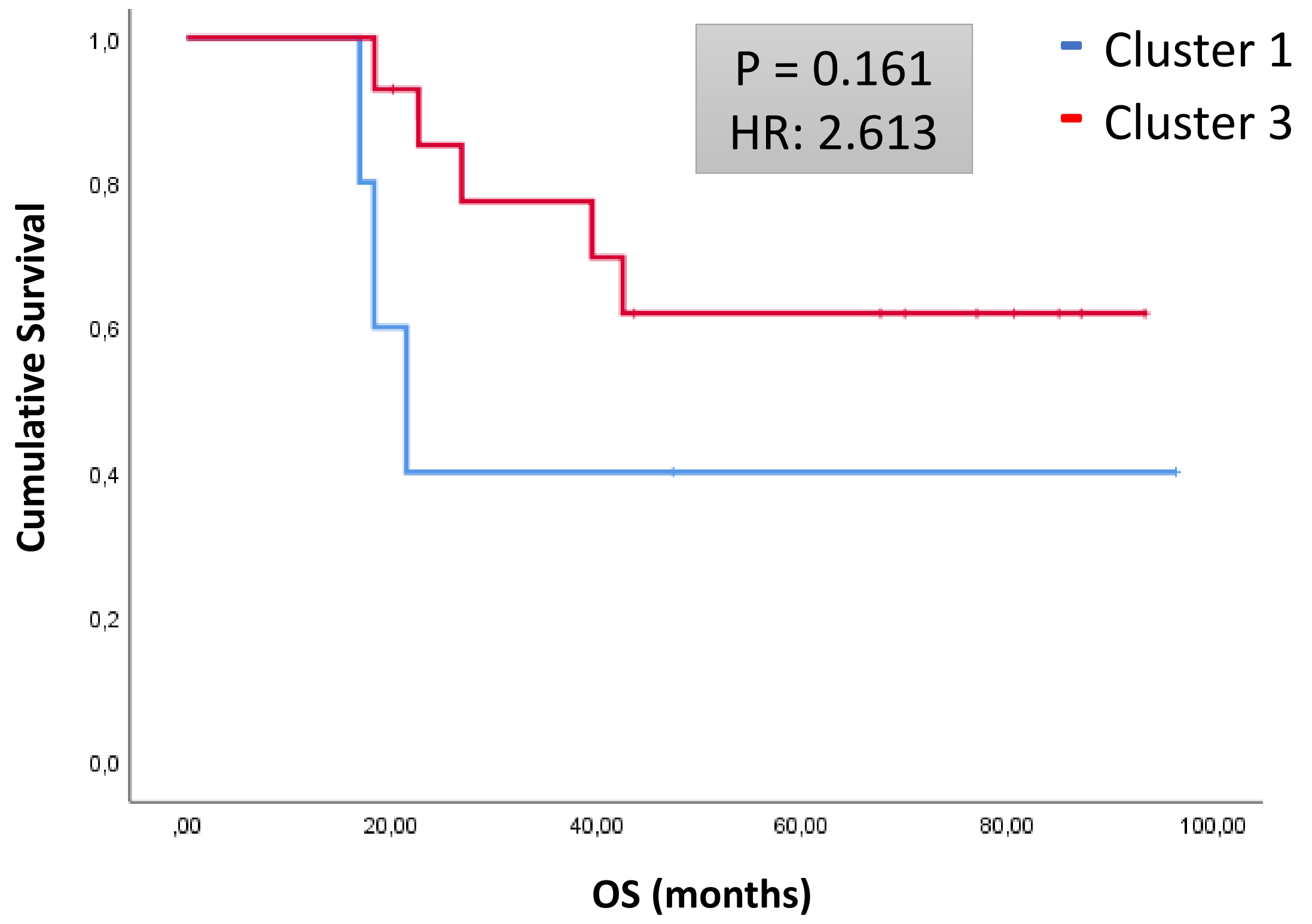


Table 1. Study population

Variable	N (=19)	%
Sex		
Male	9	47.4
Female	10	52.6
Age (years) **Median (range)**	62 (46-76)	
PS (ECOG)		
0	12	63.2
1	7	36.8
Grade		
1	2	10.5
2	17	89.5
Functioning		
No	15	78.9
Yes	4	21.1
Time from randomization to study entry (months)	40.7 (0.92-126.4)	
Treatment arm		
1	9	47.4
2	10	52.6
Metabolic Cluster		
1	5	26.3
3	14	73.7

Table 2. Multivariable Model for OS

Variable	P	HR
Metabolic Cluster	**0,067**	0,293
Sex(male vs female)	0,092	9,197
Age	0,297	1,059
Grade (G2 vs G1)	0,431	0,268
Functioning (no vs yes)	0,676	0,658
Time from randomization to study entry	0,175	0,979
Treatment arm (1 vs 2)	0,251	2,497

Conclusions/Main Findings

This study sub-analysis suggests a prognostic value of the metabolomic signature in patients with lung NETs consistent with that observed in the overall study population of patients with extra-pancreatic NET.

These data deserve further evaluation in larger populations and may lead to the improvement of the prognostic stratification of patients for clinical decisions.

Metabolomics, "OMIC" sciences, Innovative prognostic biomarkers, Lung NET, Personalized Medicine

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Future Directions for Research:

- ➢ Enlarge the sample size of Lung NET analysed by multiplatform metabolomic approach;
- ➢ Validate the achieved results in an external cohort of Lung NET.