Carcinomes de primitif inconnu: le point pour 2020

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Disclosures

- Advisory boards and symposia:
  - Amgen, Janssen Oncology, Sanofi, Astellas-Pharma, Roche

- Travel accomodations, expenses:
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Cancer of Unknown Primary (CUP): Definition

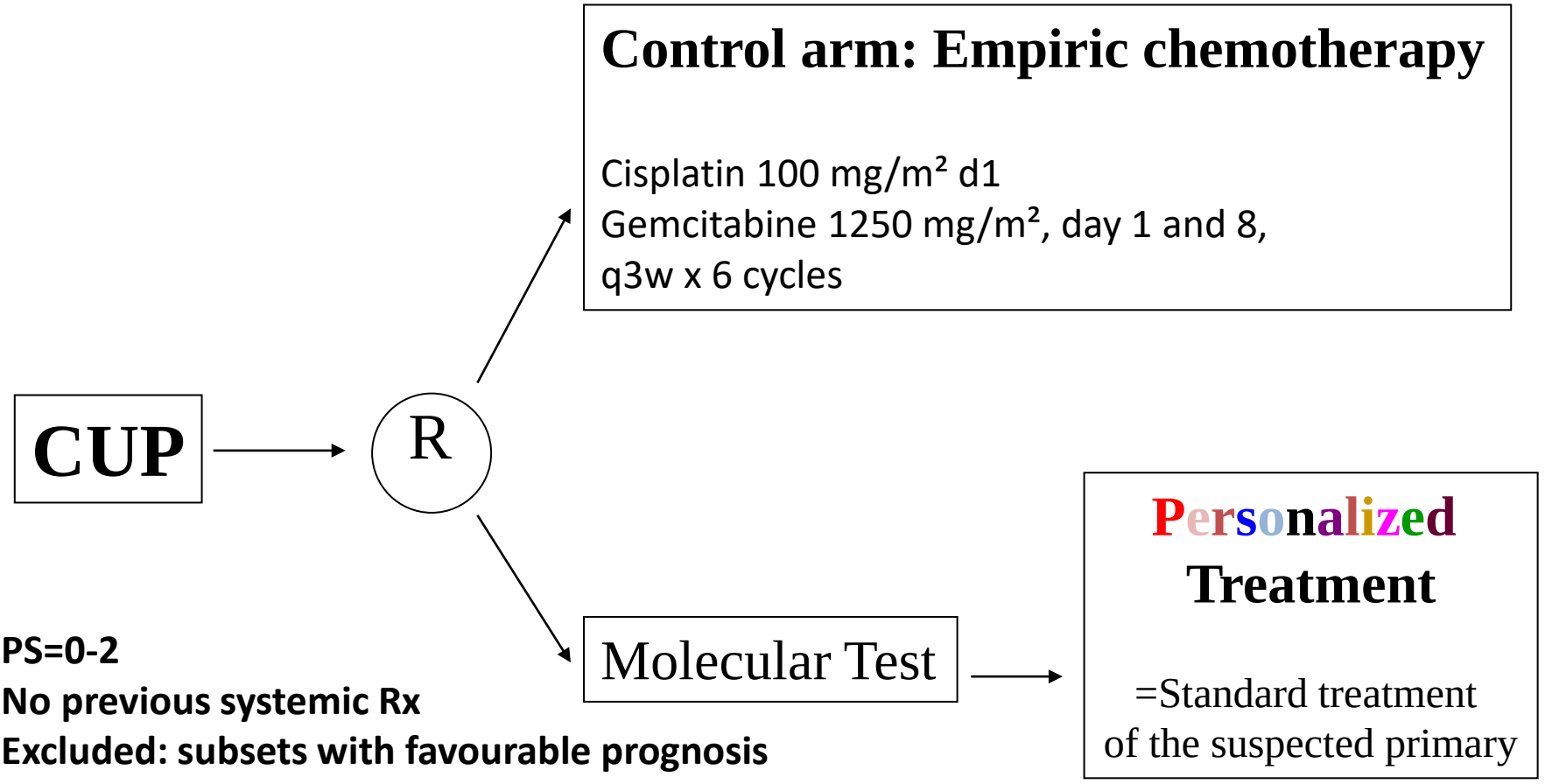
- Histologically confirmed metastases where no primary site can be confirmed **AFTER AN ADEQUATE DIAGNOSTIC EVALUATION**

- Even after a full diagnostic workup, diagnostic remains unknown in 20-50% of cases

- As carcinomas and adenocarcinomas comprise the majority of cases, CUP is often used to mean carcinoma of unknown primary

Fizazi K. Ann Oncol 2015

GEFCAPI 04 Phase III design



Fizazi K, ESMO 2019

GEFCAPI-04: Patients

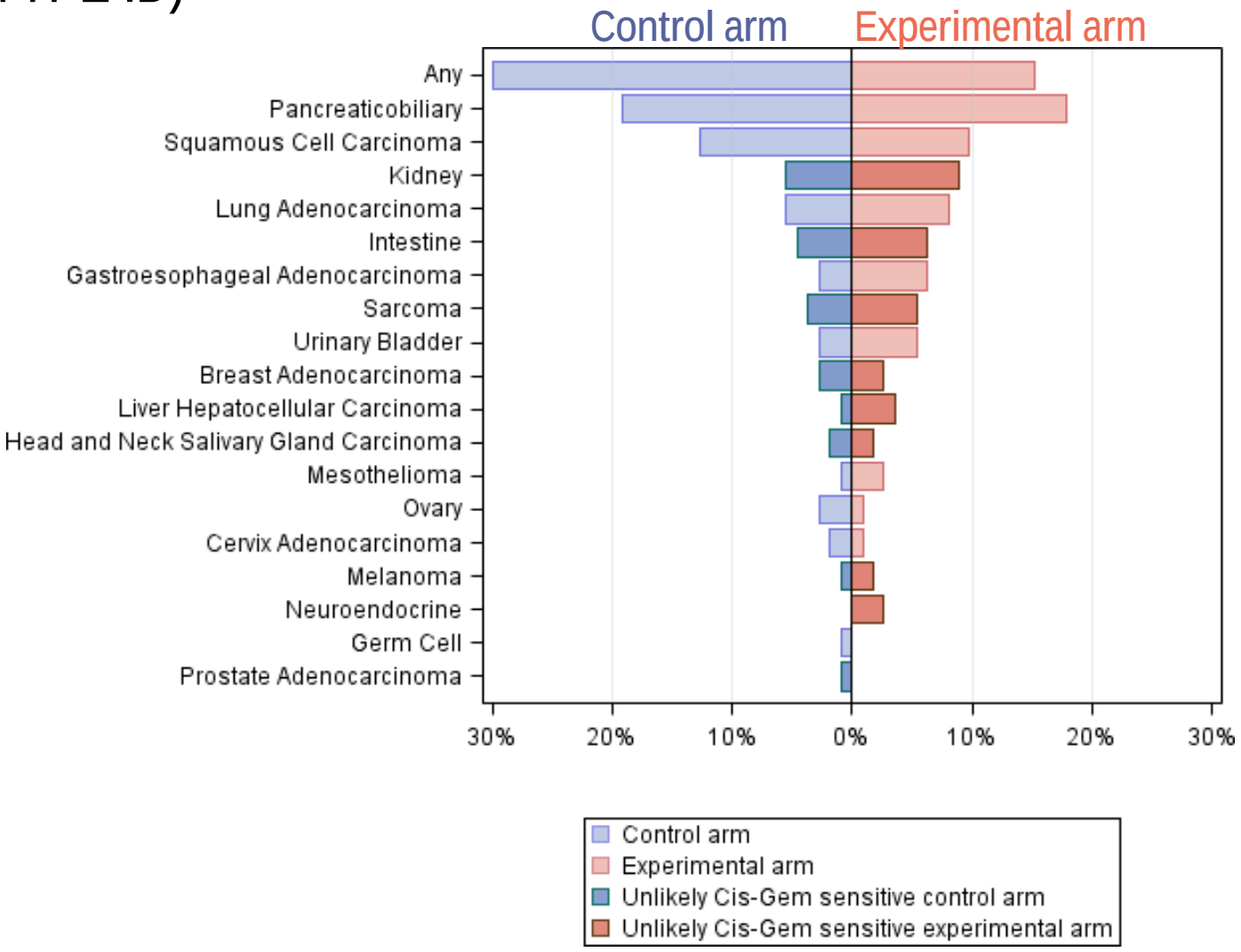
	Total	Control arm Gemcitabine/Cisplatin	Treatment of the primary suspected by molecular analysis
Intent-to-Treat population	**243**	**120**	**123**
Modified-ITT (central review available)	**223**	**110**	**113**
Cancers unlikely sensitive to cis-gem and with Biotheranostics molecular test available	**60**	**23**	**37**

Median age: 62 y (53-68), 60% male/40% female

Fizazi K, ESMO 2019

GEFCAPI-04: Suspected primary cancers

(CancerTYPE ID)



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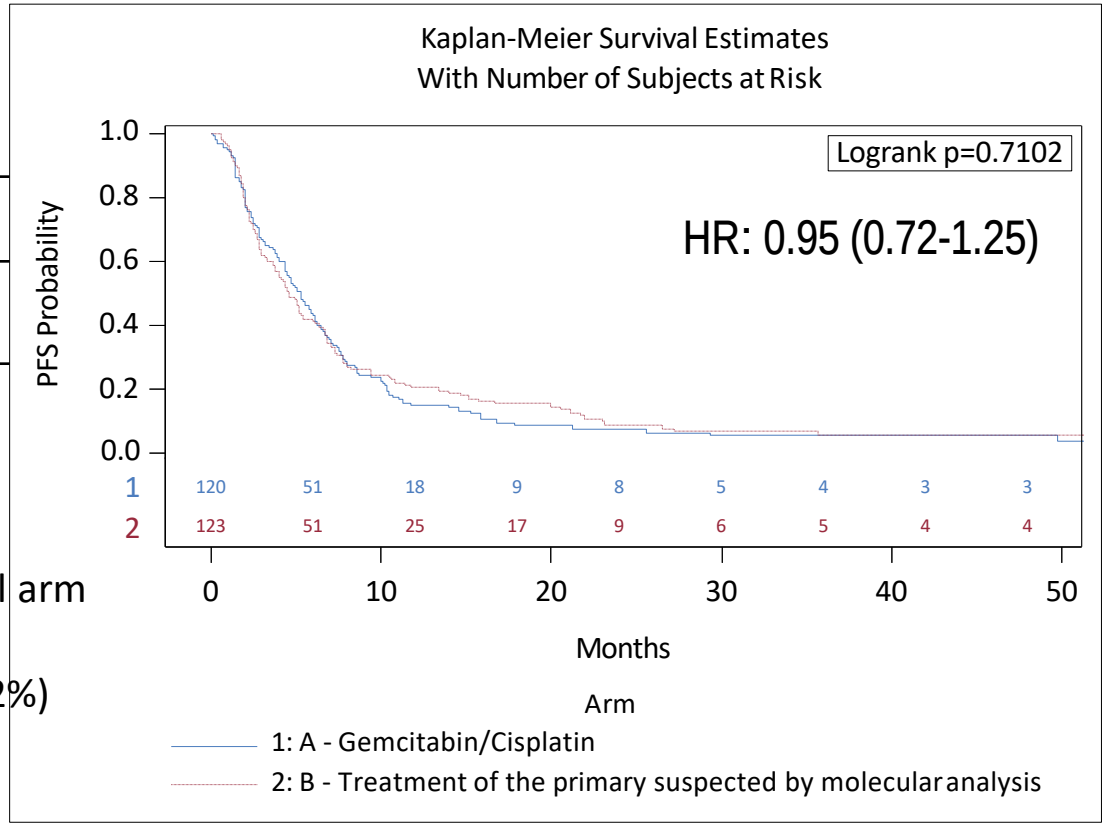
Primary endpoint: PFS (central review)

	Control arm		Experimental arm	
	Estimate	IC95%	Estimate	IC95%
Median PFS (months)	5.29	[4.30;6.24]	4.6	[3.68;6.01]
12 months PFS (%)	15.25	[9.47;22.32]	20.66	[13.98;28.26]
24 months PFS (%)	7.92	[3.86;13.87]	9.02	[4.64;15.18]
36 months PFS (%)	5.66	[2.29;11.27]	5.84	[2.41;11.48]



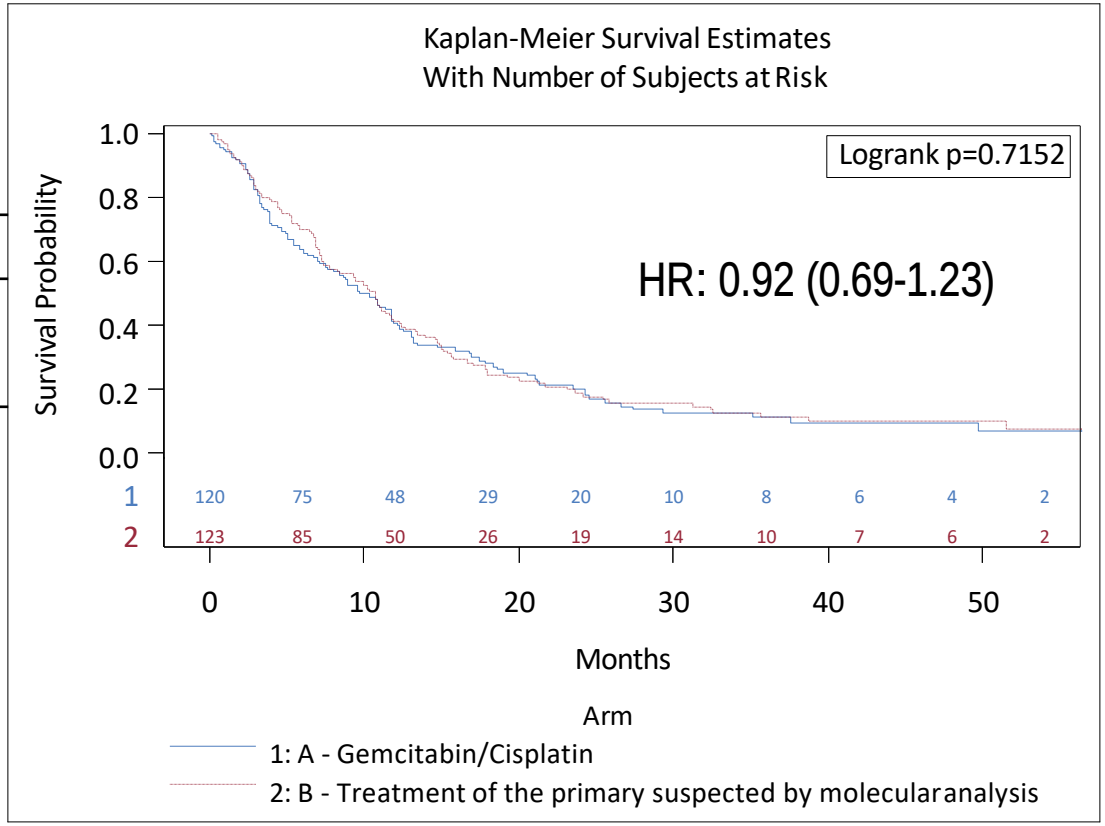
Median follow-up:
43.4 months [29.4-52.8] control arm
47.9 months [28.6-51.8] experimental arm

Central review not available: 20 pts (8.2%)

Fizazi K, ESMO 2019

Overall Survival

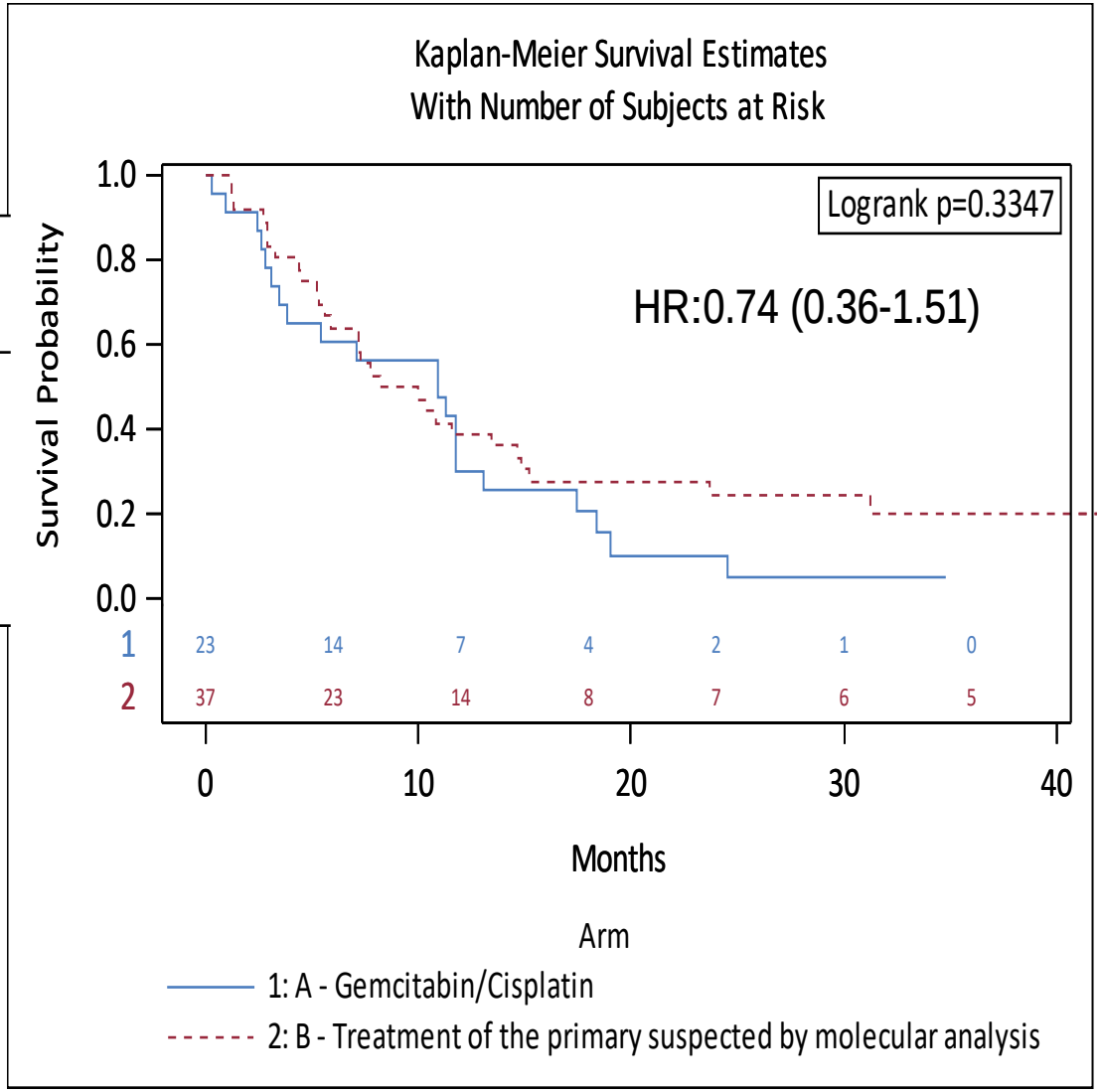
	Control arm		Experimental arm	
	Estimate	IC95%	Estimate	IC95%
Median OS (mo)	9.99	[7.06;11.96]	10.68	[7.33;11.93]
12 months OS (%)	40.68	[31.79;49.36]	41.32	[32.51;49.91]
24 months OS (%)	20.4	[13.46;28.36]	18.97	[12.34;26.70]
36 months OS (%)	11.2	[5.87;18.45]	11.41	[6.16;18.44]



Fizazi K, ESMO 2019

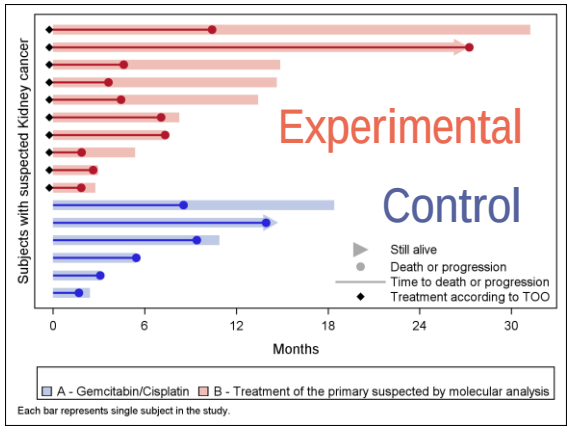
Overall Survival for patients with pre-analysis selected cancers unlikely to respond to GC

	Control arm		Experimental arm	
	Estimate	IC95%	Estimate	IC95%
Median OS (mo)	**10.87**	**[3.45;11.73]**	**9.1**	**[5.65;14.62]**
12 months OS (%)	**30.43**	**[13.54;49.28]**	**38.89**	**[23.29;54.22]**
24 months OS (%)	**10.43**	**[1.88;27.65]**	**24.31**	**[11.72;39.33]**

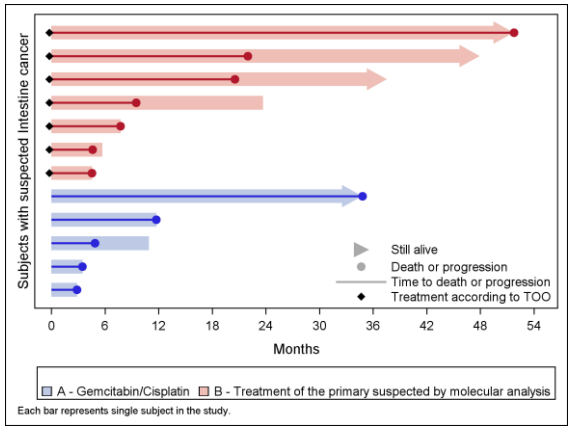


Outcomes for selected suspected cancers

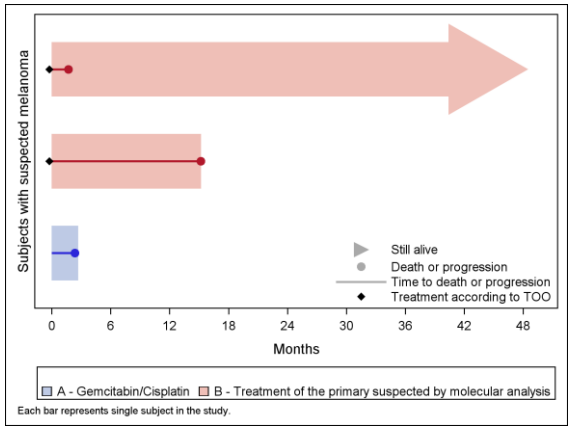
Kidney cancer



Colo-rectal cancer



Melanoma

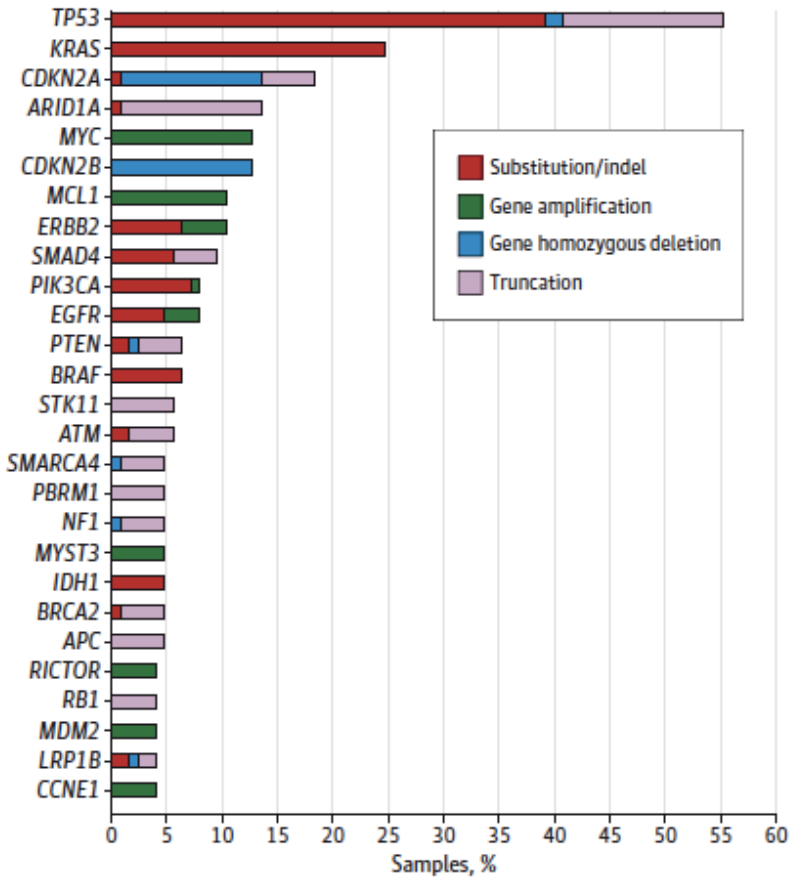


Fizazi K, ESMO 2019

- These tests can find similarities but NOT differences between cancers of similar origin
- We still do not have real effective drugs for some types of cancers
- Tailored treatment may be associated with better outcomes in suspected cancers poorly sensitive to standard chemotherapy

Comprehensive genomic profiling of carcinoma of unknown primary site

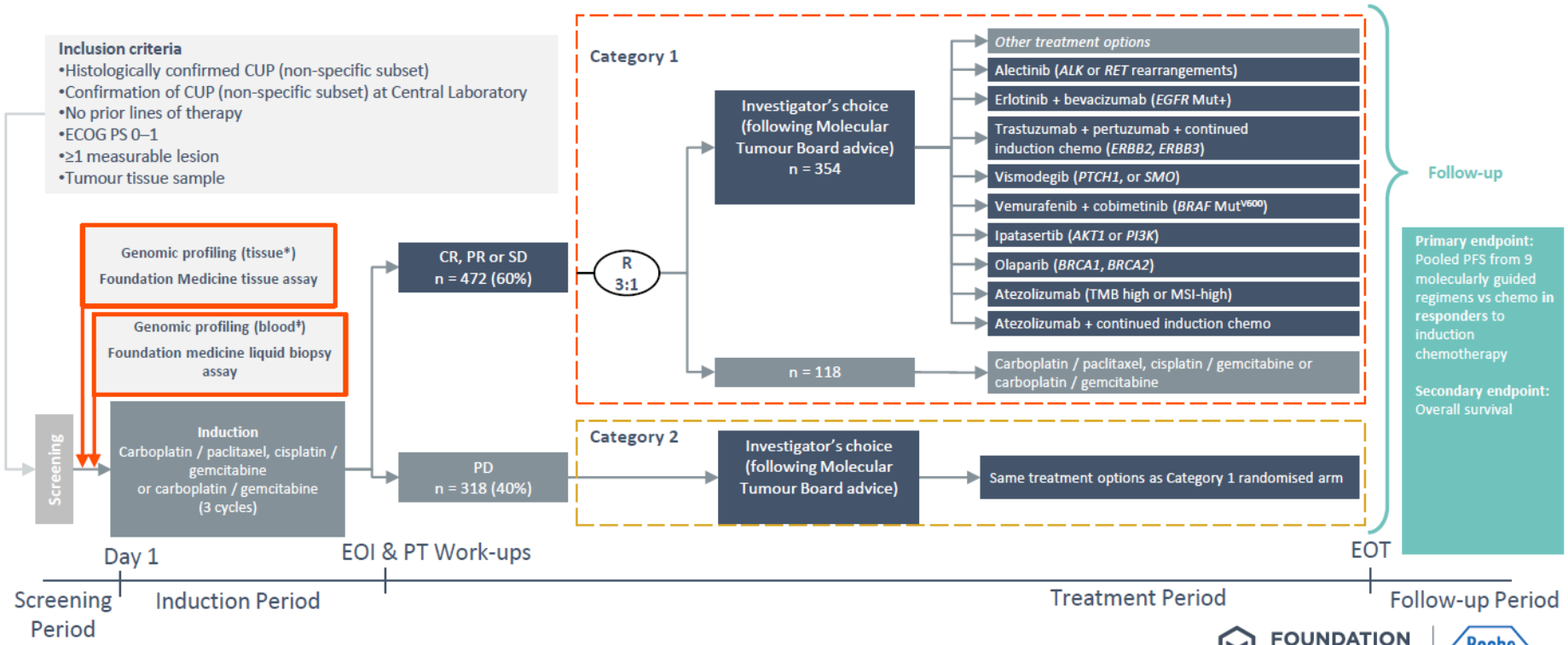
Figure 1. The Most Prevalent Genomic Alterations in 125 Samples of Adenocarcinoma of Unknown Primary Site



- Between 2% and 9% of all patients with cancer have a cancer of unknown primary (CUP).
- Nearly all CUPs studied (96%) had at least 1 genetic alteration, with a mean of 4 per tumor.
- Potentially clinically relevant genomic alterations were identified in 169 tumors (85%).
- Alterations in the RTK/Ras signaling pathway were found in 72% of adenocarcinoma CUP but only 39% of nonadenocarcinoma CUP ($P<.001$).

Ross et al., Jama Oncol, 2015

CUPISCO study design



CR: complete response; CUP: cancer of unknown primary; ECOG PS: Eastern Cooperative Oncology Group performance status; EOI: end of induction; EOT: end of treatment; PD: progressive disease; PR: partial response; PT: pre-treatment; R: randomization; SD: stable disease.

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