City of Hope

THIRD ANNUAL

ISSPP Congress 2022

International Society for the Study of Pleura and Peritoneum

PLEURAL & PERITONEAL MESOTHELIOMA

Innovative Approaches and Clinical Trials for Peritoneal Malignant Mesothelioma

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Advancing Innovative Therapies for Cancers That Invade the Peritoneum and the Pleura

Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

The off-label/investigational use of Cisplatin Doxorubicin as HIPEC/PIPAC and Immunotherapy for MPM will be discussed.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:
The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

The following CLC & IB components will be addressed in this presentation:

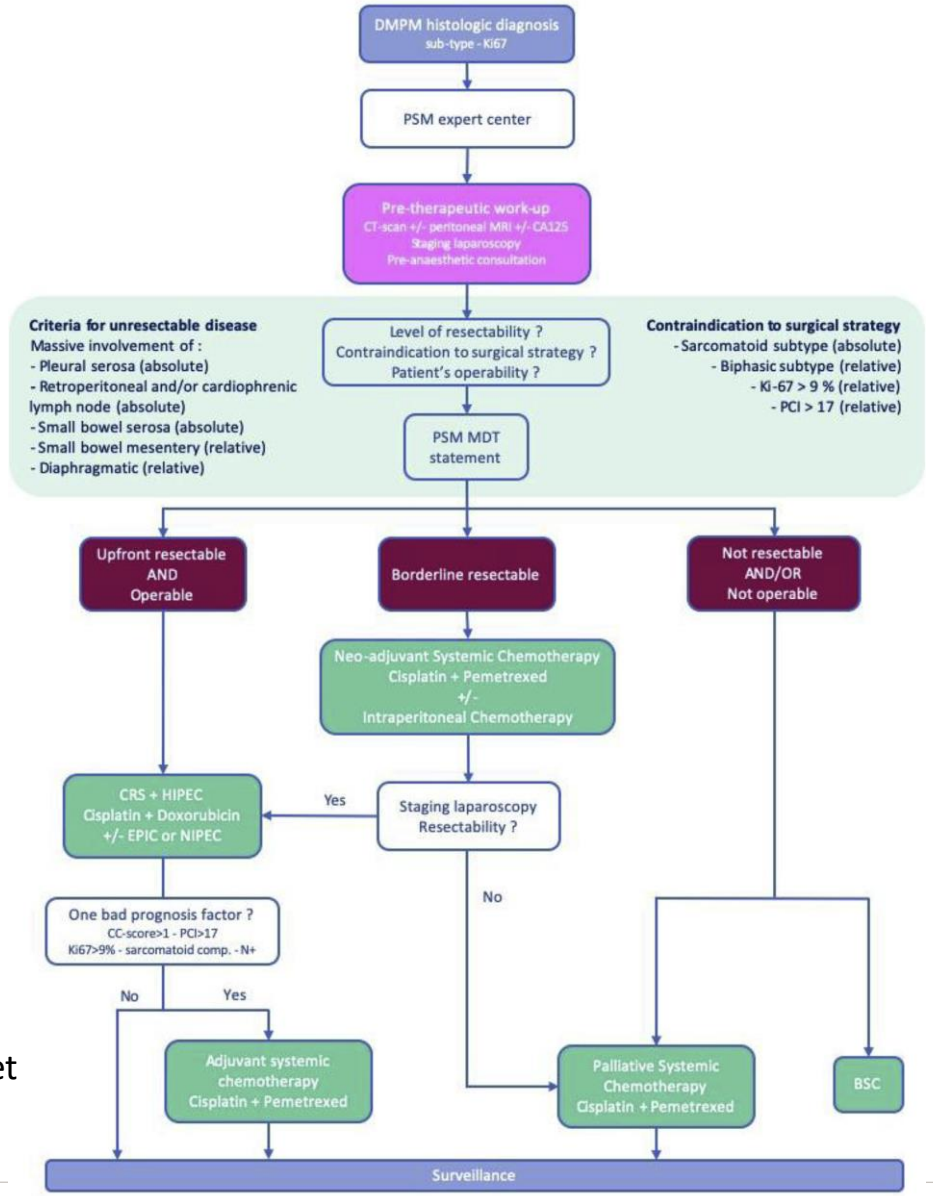
- Exposure to asbestos
- Disparities in healthcare among countries


ASBESTOS

What is acquired

- Since 2018 –PSOGI consensus for the treatment of DMPM[1]

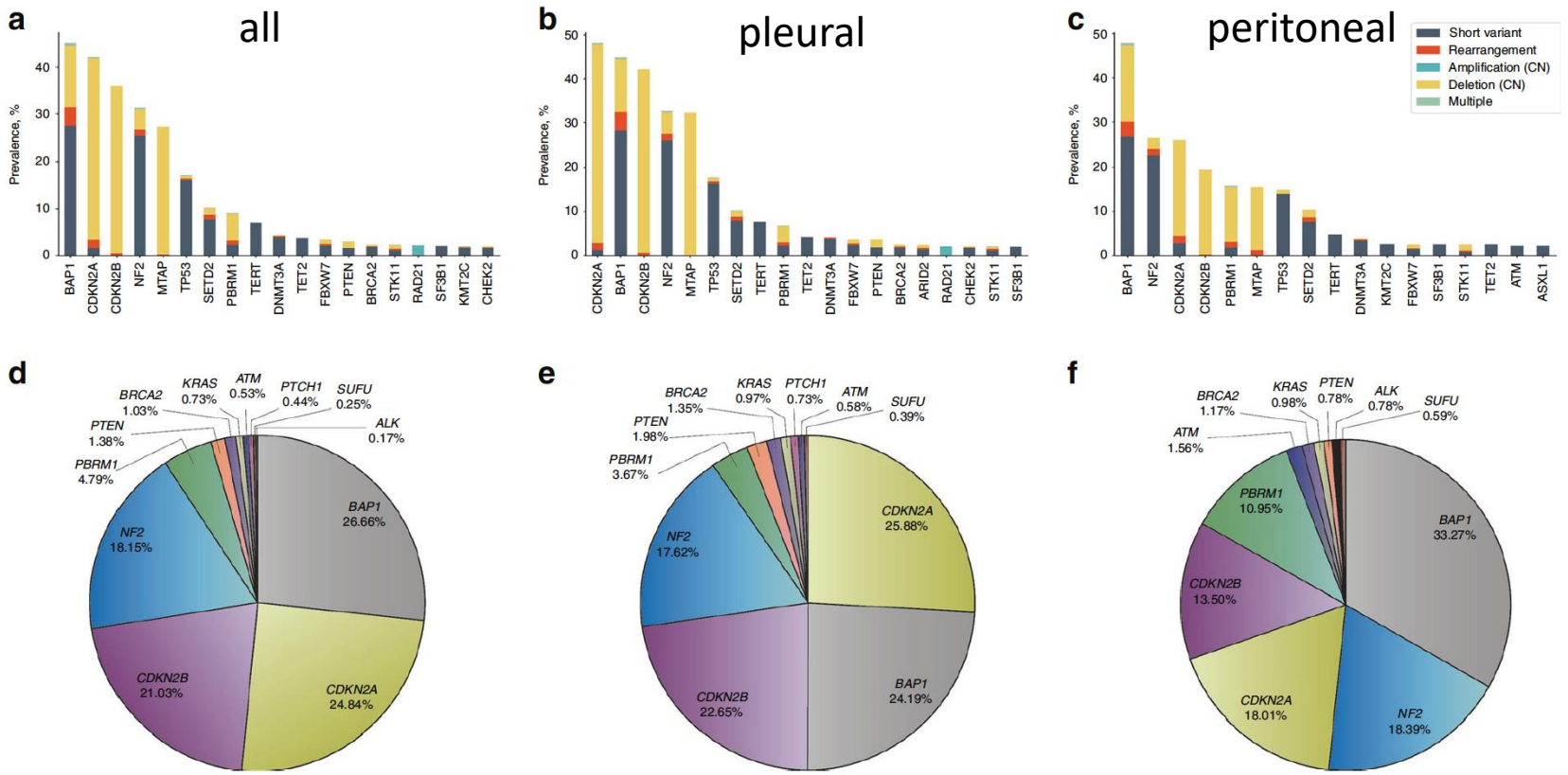
  - OS for resectable DMPM is **53** months[2]
  - Unresectable DMPM : with sCT alone– **13** months [3,4]
  - High rate of unresectable disease[5]
  - Complex immune-milieu and a pro-inflammatory microenvironmentwith 50-60% cases expressing PD-L1[6]



[1] Kusamura S et al, EJSO, 2020; [2] Yan TD et al, JCO, 2009; [3] Janne PA, Clin Lung Canc, 2005; [5]Miura JT et al, ASO, 2014; [6]Chapel DB et al, Hum Pathol, 2019


ROOSEVELT TEN CENT PIECE
SALIVARY GLAND
PREMOLARS
ASBESTOS
RADIUM
MOLARS
CANINE
INCISORS
TEETH
TEETH
AN ENBALMED EGYPTIAN KING
MEMPHIS
GIZEH
TURA
HELIOPOLIS
TANIS
TRUE
FALSE
SALIVARY GLAND
JUPITER
LIBERTY

Disease characterization



Hiltbrunner et al, BJC, 2022

Genomic landscape of mesothelioma based on 1113 pleural Meso and 355 DMPM – Foundation One

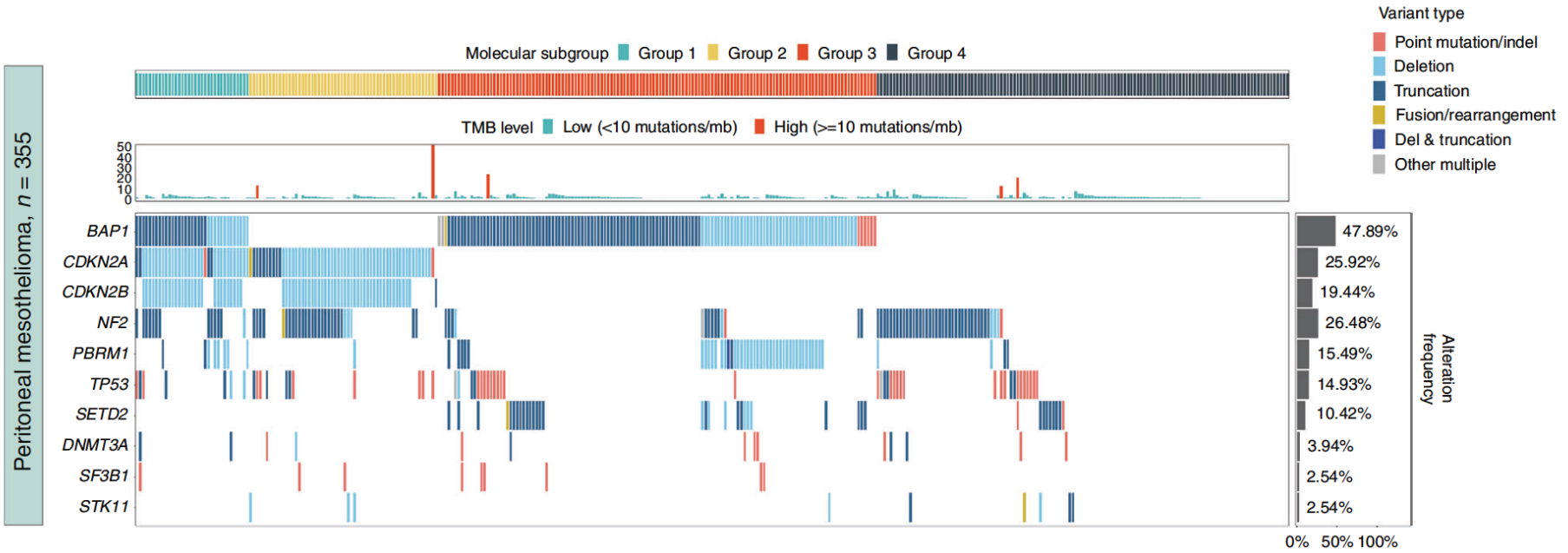


Table 2. Selected alterations in peritoneal mesothelioma patients split according to the groups defined in the tiles plot.

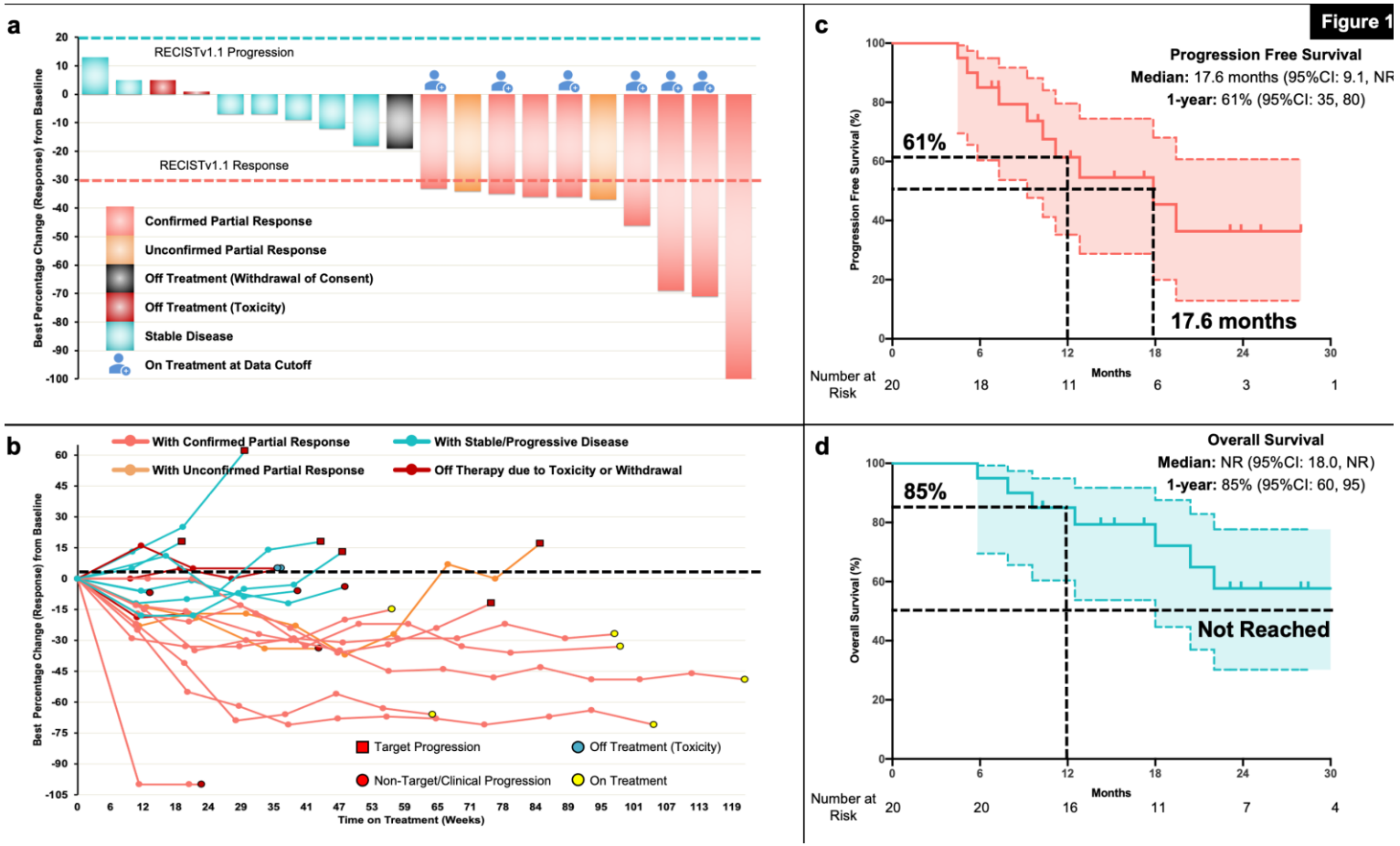
Gene	Group 1 (alterations in *CDKN2A/B, BAP1*), $n = 35$	Group 2 (only alterations in *CDKN2A/B*), $n = 58$	Group 3 (only alterations in *BAP1*), $n = 135$	Group 4 (no alterations in *CDKN2A/B, BAP1*), $n = 127$
NF2	37.14%	48.28%*	10.37%*	30.71%
MTAP	72.22%	38.46%	1.64%	1.75%
TP53	20.00%	18.97%	10.37%	16.54%
SETD2	0.00%	0.00%	20.74%*	7.09%
PBRM1	22.86%	1.72%*	31.11%*	3.94%*
TERT	3.13%	9.26%	3.31%	4.55%
TET2	2.86%	3.45%	1.48%	3.15%
DNMT3A	5.71%	3.45%	3.70%	3.94%
PTEN	0.00%	1.72%	0.00%	2.36%
BRCA2	5.71%	0.00%	2.96%	0.00%
STK11	0.00%	5.17%	0.74%	3.94%
KRAS	0.00%	5.17%	0.00%	1.57%
RB1	0.00%	0.00%	0.74%	3.15%

Selected genes had a prevalence >1% and can be targeted with available drugs. Chi-square test was used to test for statistically significant; significant values compared to the entire pleural mesothelioma cohort are indicated as *$P < 0.05$.


STATIC
ASBESTOS
LEAD

Innovative treatments - Immuno

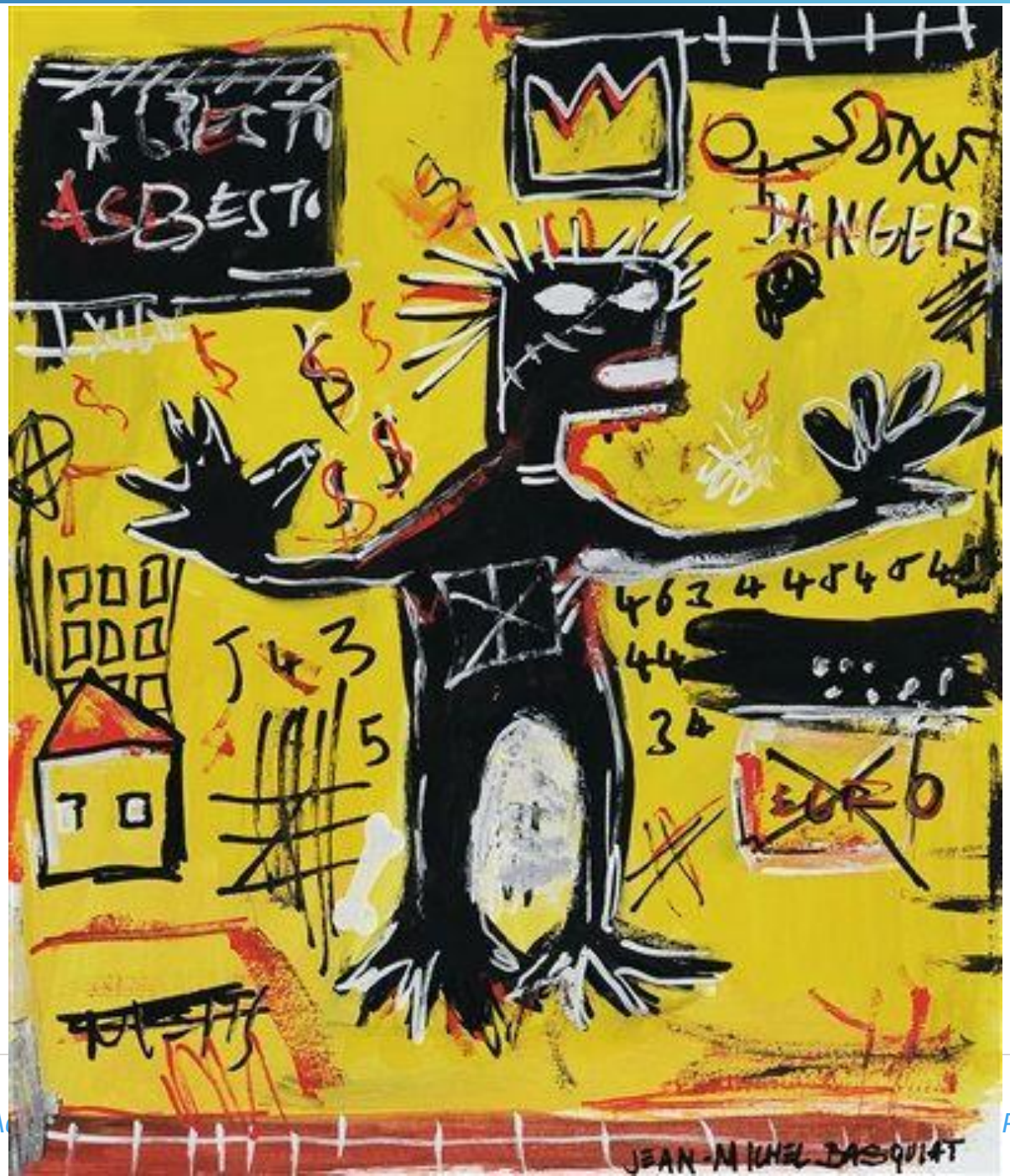
- Phase II: Atezo + Beva – 20 patients
- ORR: 40%
- PFS: 17.6 mo



Raghav K et al. AACR, 2021

Innovative treatments - Immuno

Agent	Type	Participants	Setting	Main endpoint	Center
Nivo/Ipi	Phase II	37	Resectable MPM	Major pathologic response rate	Chicago – K. Turaga
Atezo/Beva +sCT vs Beva+sCT	Phase II RCT	66	Resectable and unresectable induction ttt	Response rate	Boston Mayo– AS Mansfield


ASBESTOS
DANGER
JEAN-MICHEL BASQUIAT

Innovative treatments - IP

Open access Protocol

BMJ Open

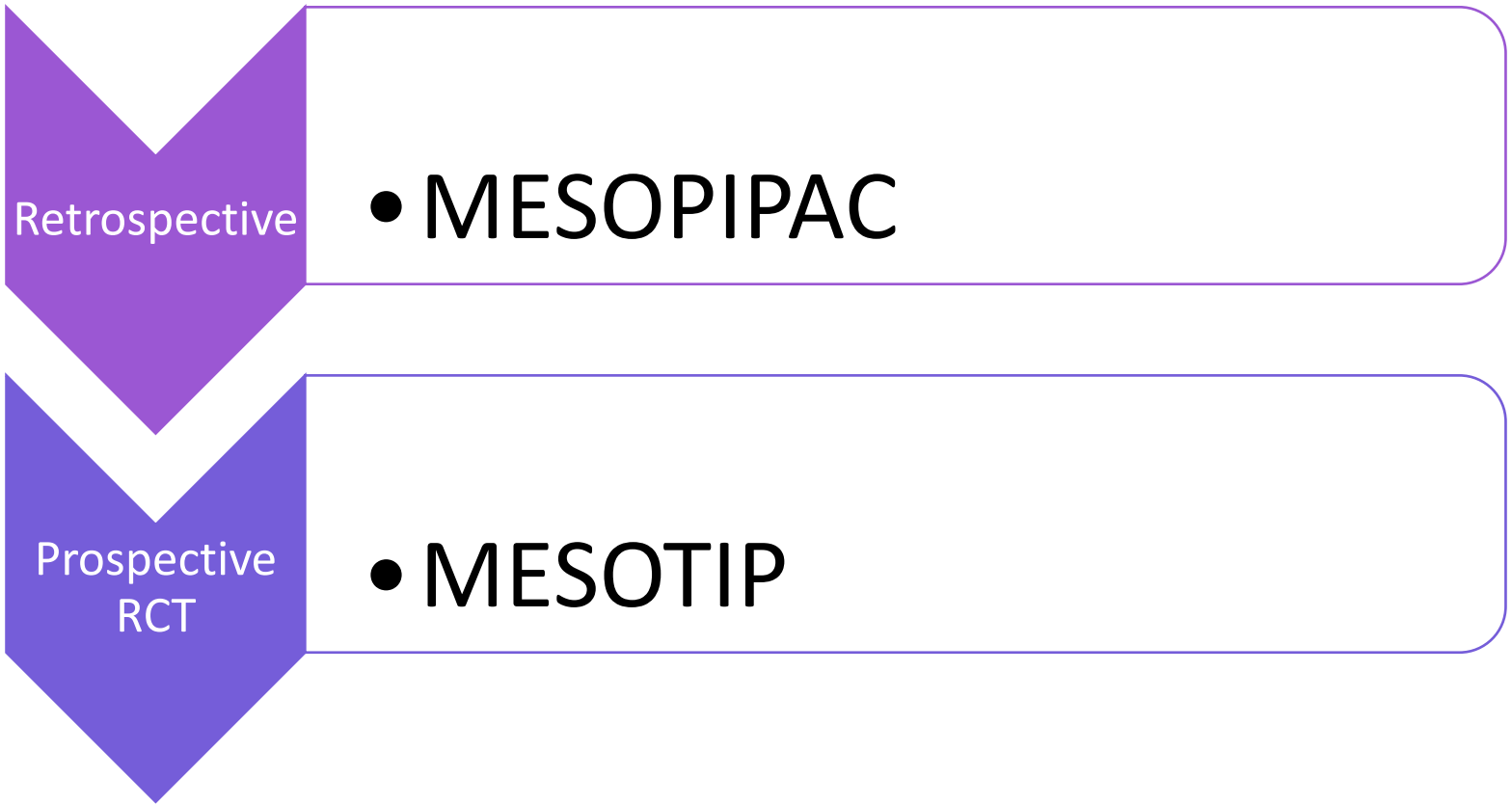
Intraperitoneal paclitaxel for patients with primary malignant peritoneal mesothelioma: a phase I/II dose escalation and safety study – INTERACT MESO

Job P van Kooten,[1] Michelle V Dietz ,[1] Niels A D Guchelaar,[2] Alexandra R M Brandt-Kerkhof,[1] Stijn L W Koolen,[2,3] Jacobus W A Burger,[4] Ron H J Mathijssen,[2] Cornelis Verhoef,[1] Joachim G J V Aerts,[5] Eva V E Madsen[1]

Paclitaxel in monotherapy – no sCT

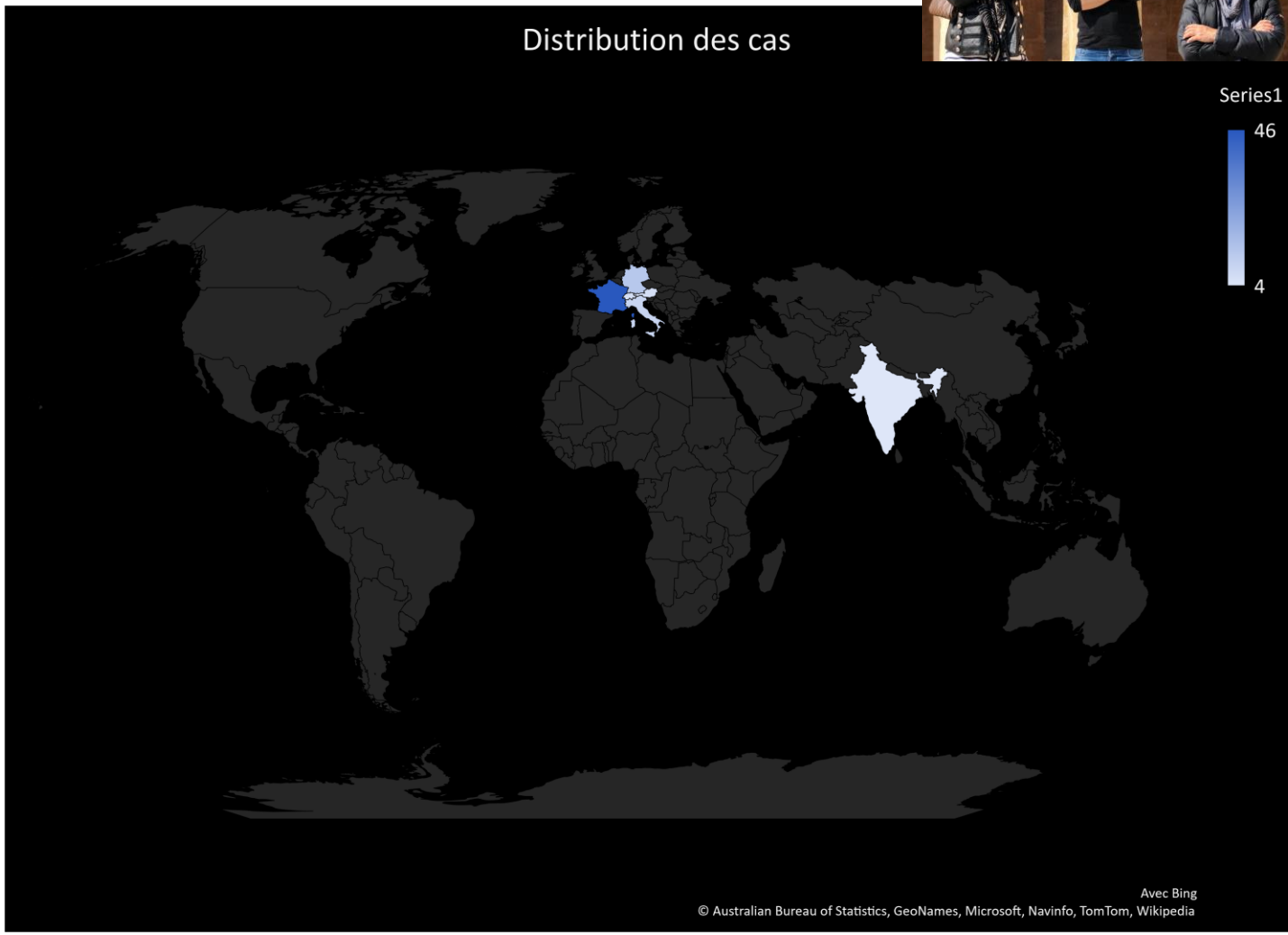
No clear criteria for defining irresectability

Innovative treatments - PIPAC



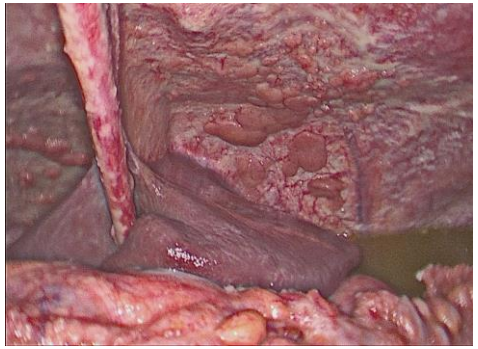
PIPAC cohort studies initiative

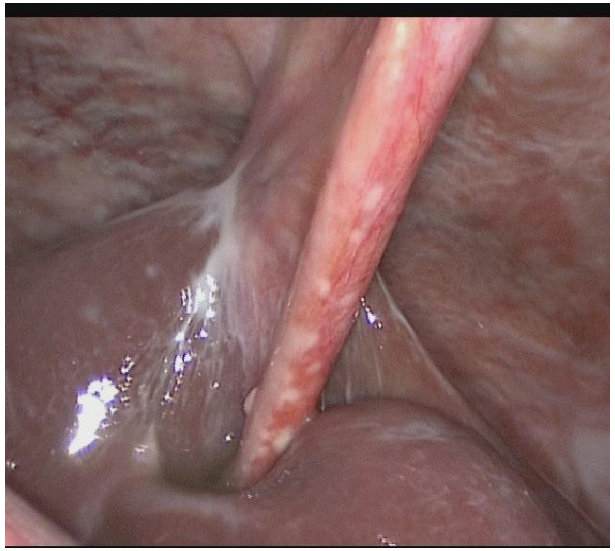
- 26 invited expert centers (>60 cases in october 2019)[1]
- 19 centers agreed to participate
- Only 15 centers for DMPM (8 countries) – 6 in FR
- 13 centers are part of PSOGI/ESPSO – expertise in DMPM
- 2 centers only account for 8 cases



[1]Sgarbura O et al, EJSO, 2020

Outcomes and statistics





Outcomes:

- Overall survival – date of PIPAC1/ date of diagnosis
- Progression free survival
- Response to treatment: clinical (symptoms), visual (PCI), radiological (RECIST), histological

STATA v16.0 (StataCorp LLC, Tx, USA)

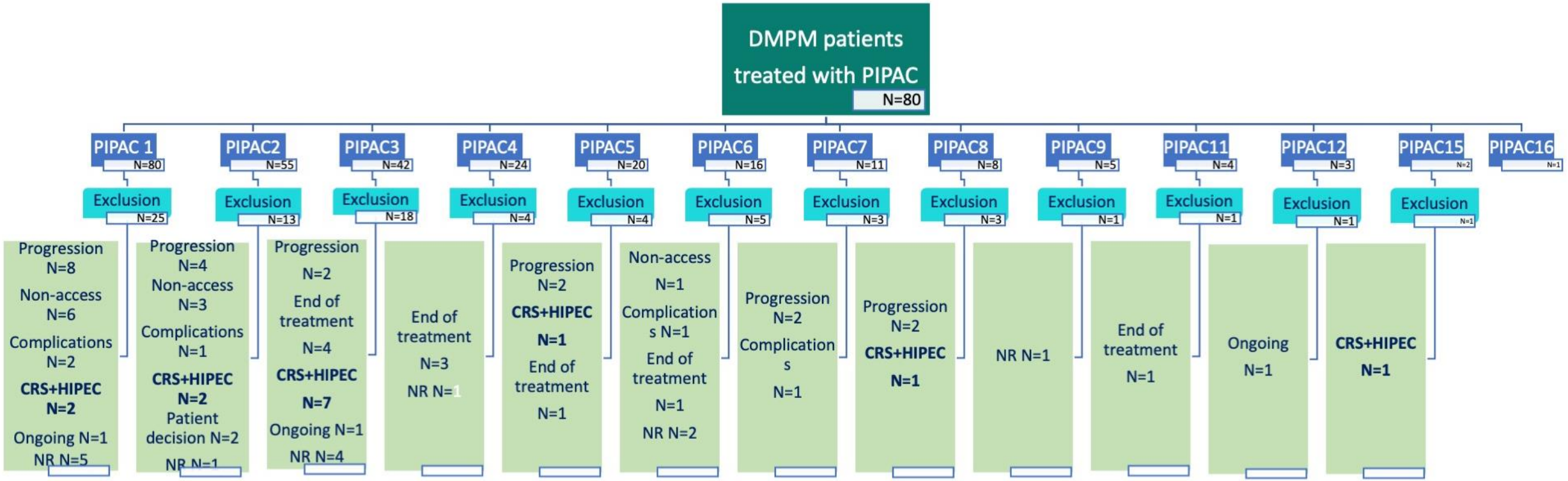
- Non-parametric tests
- Survival-analysis
- Uni- and multi-variate analysis

Results

- 80 patients – 61% male; median age 68
- Median number of PIPAC: 3
- Median follow-up from DMPM diagnosis: 29.1 months (CI 95% [19.4; 45])
- From PIPAC1: 20.2 months (CI 95% [13.1; 29.6])
- Median PCI 28 (1-39)
- Symptoms pre-PIPAC 75%
- 2nd line of treatment: 67%
- 42 pp-patients (≥3 PIPACs)
- bi-directional treatment in 35pts (43%)

No difference of characteristics for pp-patients vs the rest on any other characteristic except for number of cycles

Sgarbura O et al, submitted



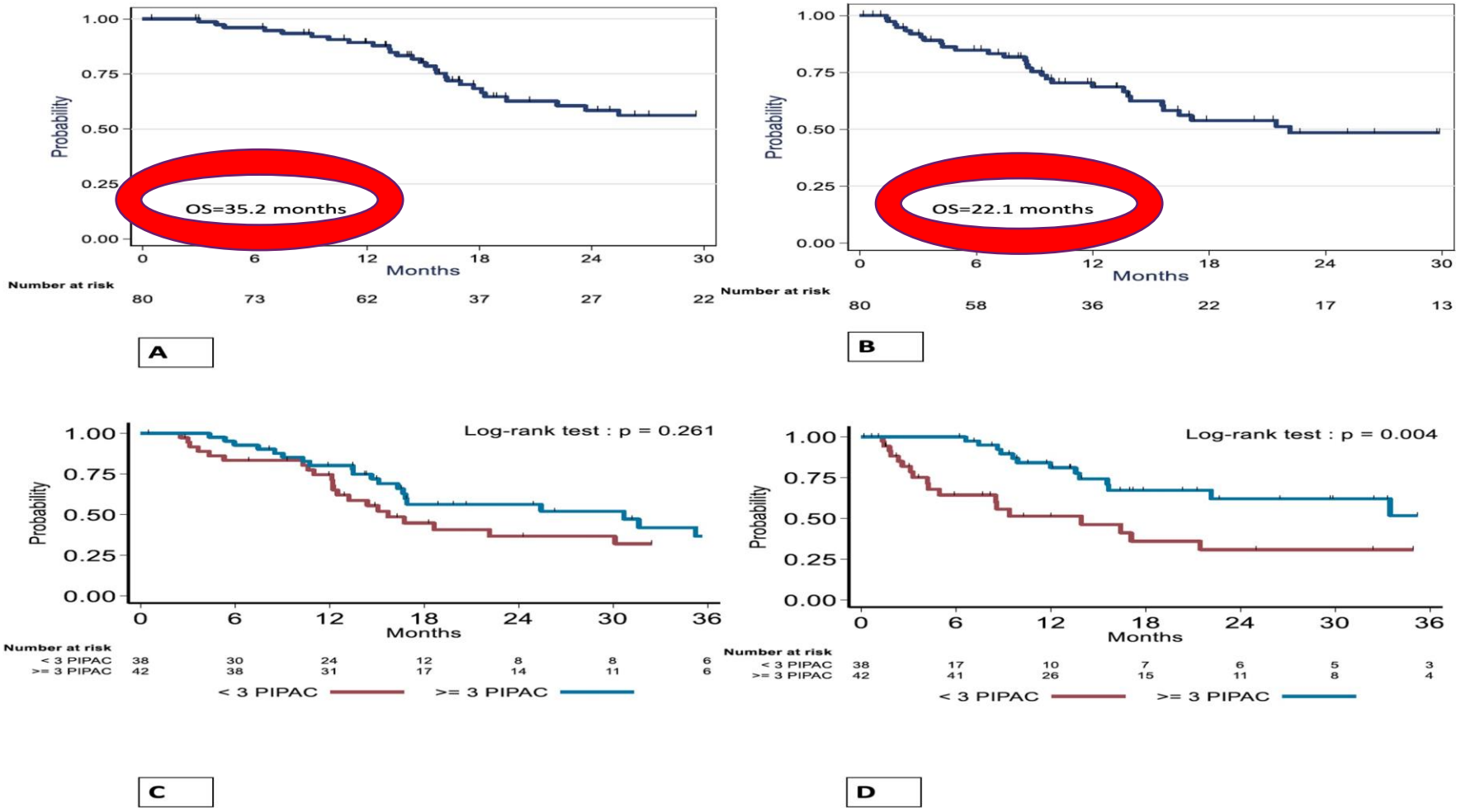
Sgarbura O et al, submitted

Response to treatment

Parameter		PP cohort (n=42) At baseline	PP cohort (n=42) ≥3 PIPACs	*P* value
RECIST	Partial response/stable	-	31 (77.5%)	-
	Progression	-	9 (22.5%)	
PRGS	1-2	-	28 (66.7%)	-
	3-4	-	14 (33.3%)	
Cytology	Positive	38 (74.5%)	16 (51.6%)	**0.025**
	Negative	13 (25.5%)	15 (48.4%)	
ΔPCI (PIPAC1 *vs* 3)	≥ 3 decrease	-	12 (33.3%)	-
	<3 decrease or increase	-	24 (66.7%)	
Any Symptoms	Yes	58 (74.4%)	24 (64%)	0.3
	No	20 (25.6%)	13 (36%)	

Sgarbura O et al, submitted

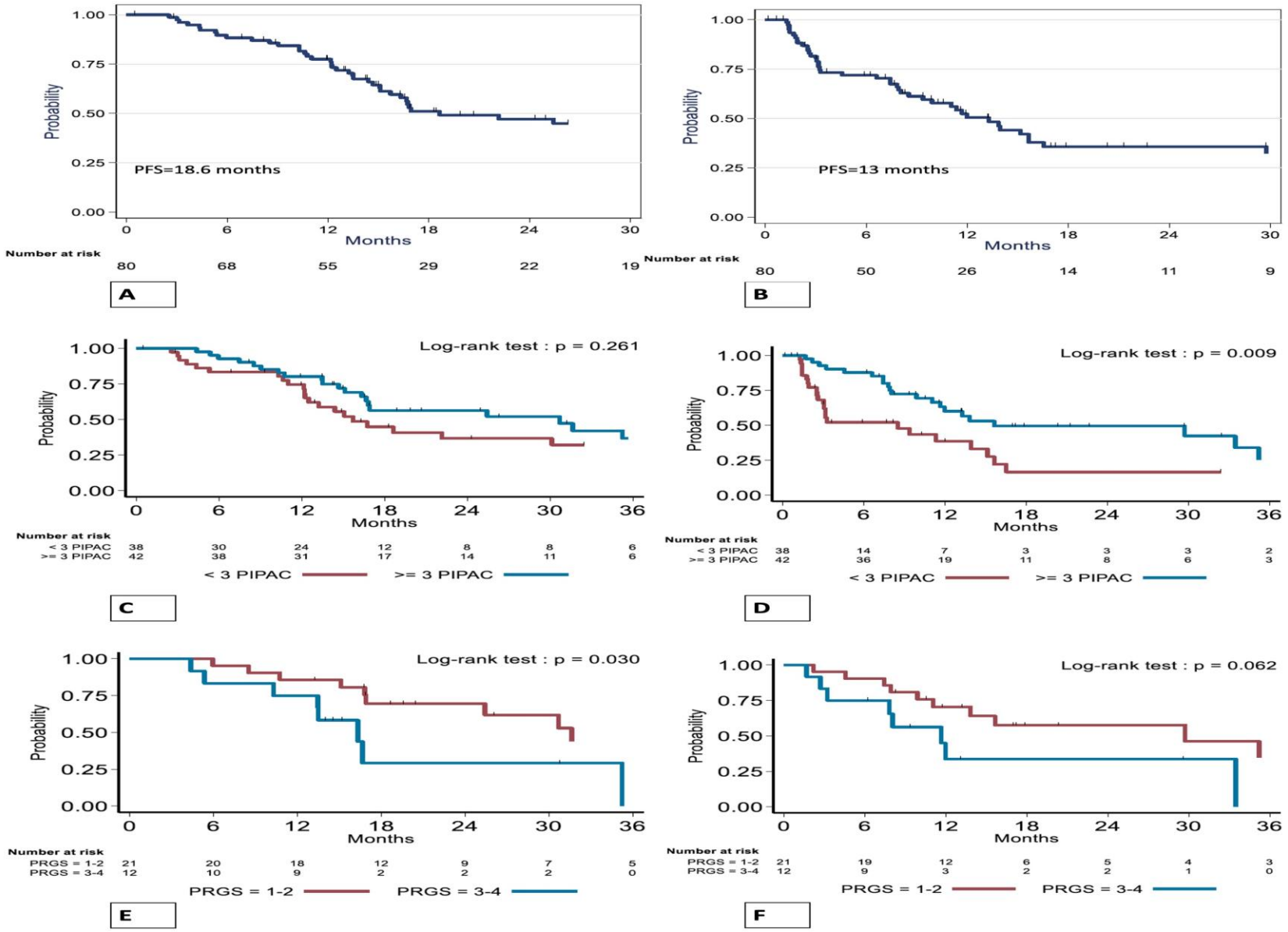
Overall survival



Median OS for resected patients: 49.6 months (CI 95% [37.6; 61.6].

Sgarbura O et al, submitted

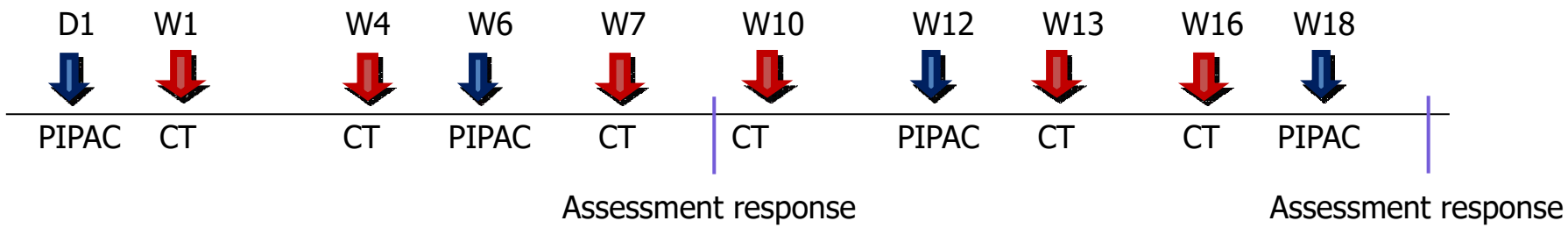
Progression free survival



Sgarbura O et al, submitted

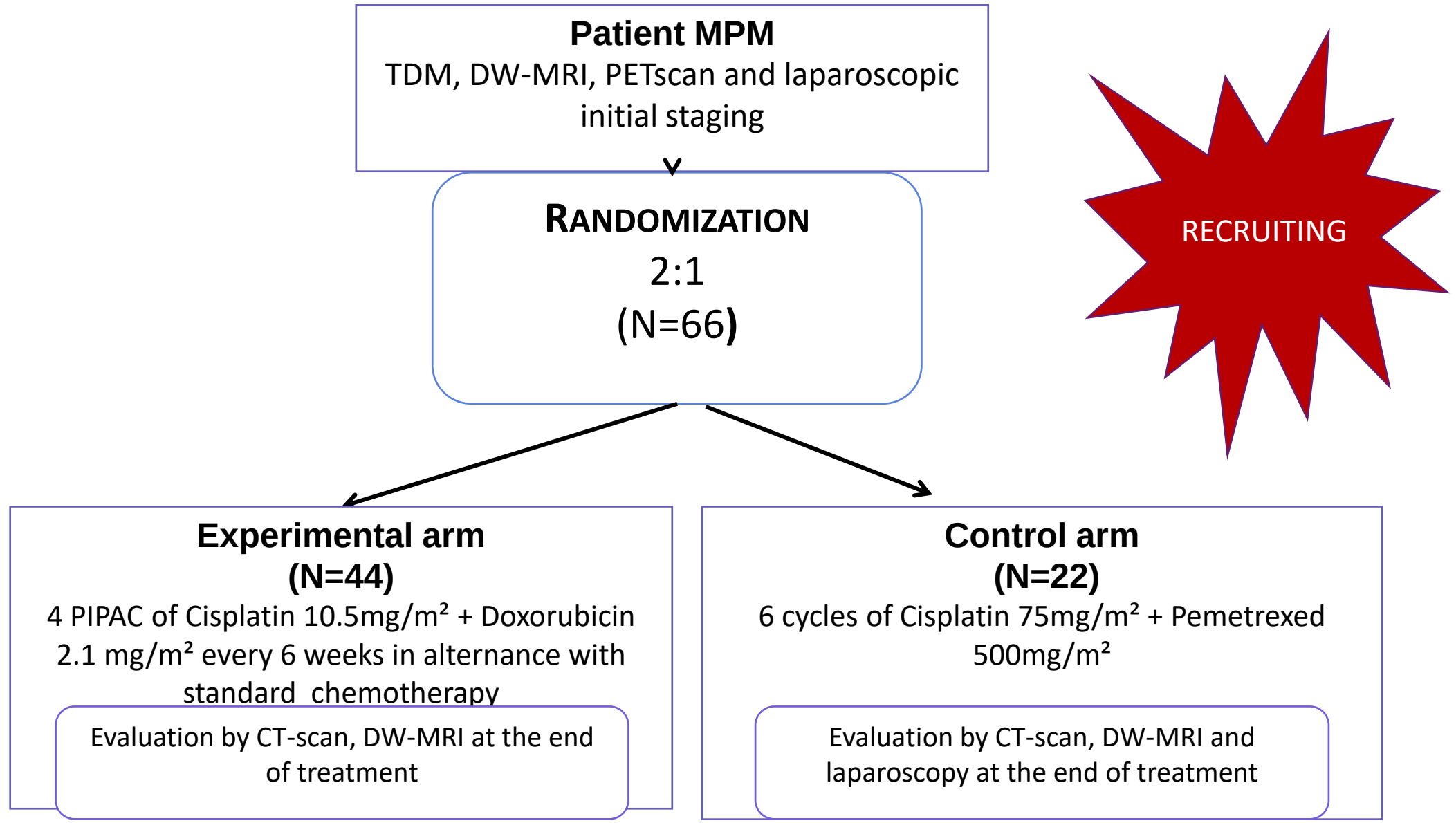
MESOTIP

Phase II randomized non-comparative trial concerning the use of PIPAC in alternance with systemic chemotherapy in the first line of treatment of unresectable MMP[1]



Institut régional du Cancer Montpellier | Val d'Aurelle

[1] Sgarbura et al, P&P, 2019


Patient MPM
TDM, DW-MRI, PETscan and laparoscopic initial staging
RANDOMIZATION
2:1
(N=66)
RECRUITING
Experimental arm
(N=44)
4 PIPAC of Cisplatin 10.5mg/m² + Doxorubicin 2.1 mg/m² every 6 weeks in alternance with standard chemotherapy
Evaluation by CT-scan, DW-MRI at the end of treatment
Control arm
(N=22)
6 cycles of Cisplatin 75mg/m² + Pemetrexed 500mg/m²
Evaluation by CT-scan, DW-MRI and laparoscopy at the end of treatment


INTOXICATED
ST. LOUIS
MEAT BALLS
EGGS
EGGS
EGGS
ESSO
MILK
ASBESTOS

Innovative treatments - maintance

RECRUITING

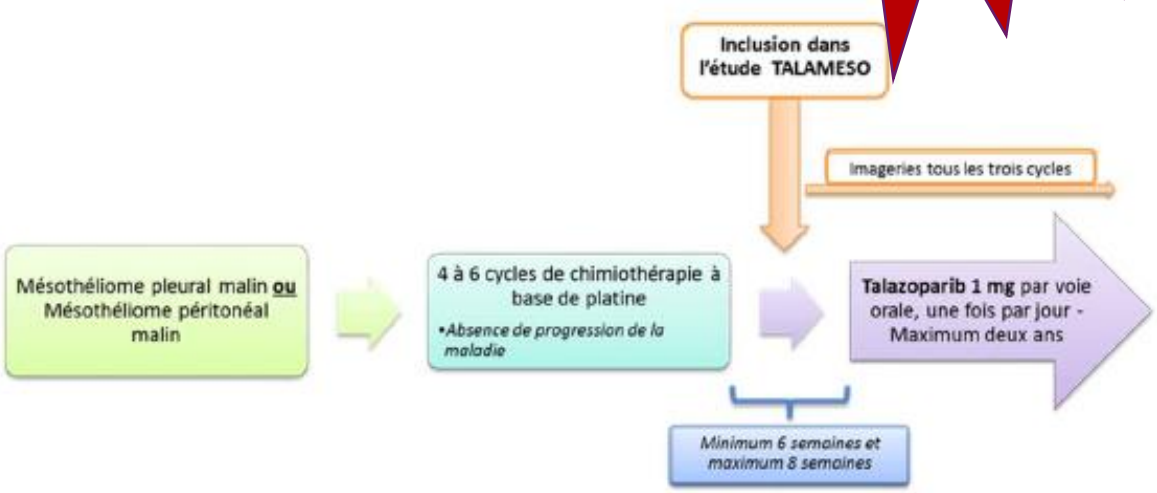
TALAMESO – maintenance treatment with Talazoparib – ph II

3 cohorts:

A – pleural mesothelioma

B1 – unresectable peritoneal DMPM (14 pts)

B2 – resectable peritoneal DMPM (9 pts)



Primary endpoint

% of patients without progression at 6 mo after the start of the treatment with Talazoparib

The treatment:

4 to 6 cycles Pt-based (Cisplatin - Pemetrexed etc) followed by 2 y maintenance treatment with Talazoparib (PARP 1 and 2 inh) : 1mg/day po

Thank you!