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Cancer cell-specific MoA

- Tumour cells generate elevated levels of reactive oxygen species
- Peroxide scavenging enzyme peroxiredoxin 3 metabolizes ~ 90% of mitochondrial ROS, primarily H₂O₂
- PRX3 is upregulated in approximately 50% of cancers
- Genetic knock down of PRX3 in human tumour cells results in apoptosis
- Mitochondria of malignant mesothelioma cells have altered metabolic function that supports tumour growth
- 90% of mesotheliomas at diagnosis and ~15% of late-stage cancers exhibit pleural effusion
- The only licensed therapies for pleural mesothelioma are systemic drugs for ‘unresectable’, late-stage disease

RSO-021 - a novel formulation of thiostrepton

RSO-021 inhibits PRX3, which causes a rise in H₂O₂ (oxidative stress)

Cancer cell

While normal cells can metabolize increased H₂O₂...

Normal cell

...for cancer cells the build-up of H₂O₂ is lethal!

Cancer cell

MoA illustration taken from materials used to inform trial participants.

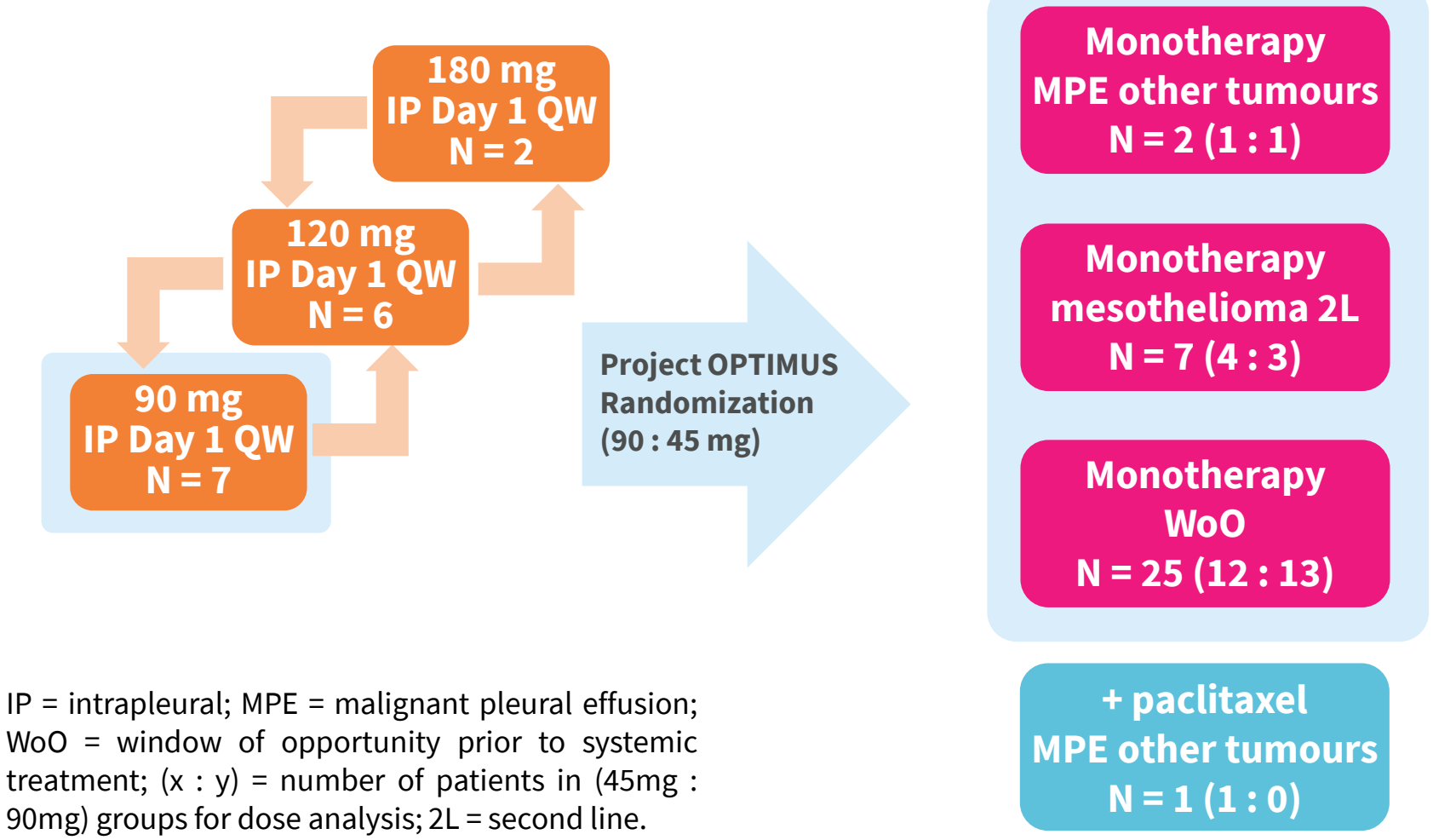
- RSO-021 is administered intrapleurally, QW via an intrapleural catheter
- Prior to RSO-021 administration, pleural effusions are drained to dryness, per standard of care

Phase 1-2 study design

- Primary Objective:**
- Assess safety, tolerability and toxicity profile of RSO-021 in patients with pleural effusion from any solid tumour type and mesothelioma
- Secondary Objectives:**
- Establish systemic and local PK
 - Preliminary anti-tumour activity
 - Evaluate respiratory function
 - Redox status in translational samples

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Phase 1 escalation



- In phase 1 escalation
 - efficacy signals at 90 mg
 - DLTs at higher doses
- Per Project Optimus, 45 and 90 mg explored in phase 2 expansions
 - This analysis includes patients from phase 1 - 2 who received 45 or 90 mg QW
 - 24 patients (58.5%) had no prior anti-cancer therapy

Largely typical mesothelioma population

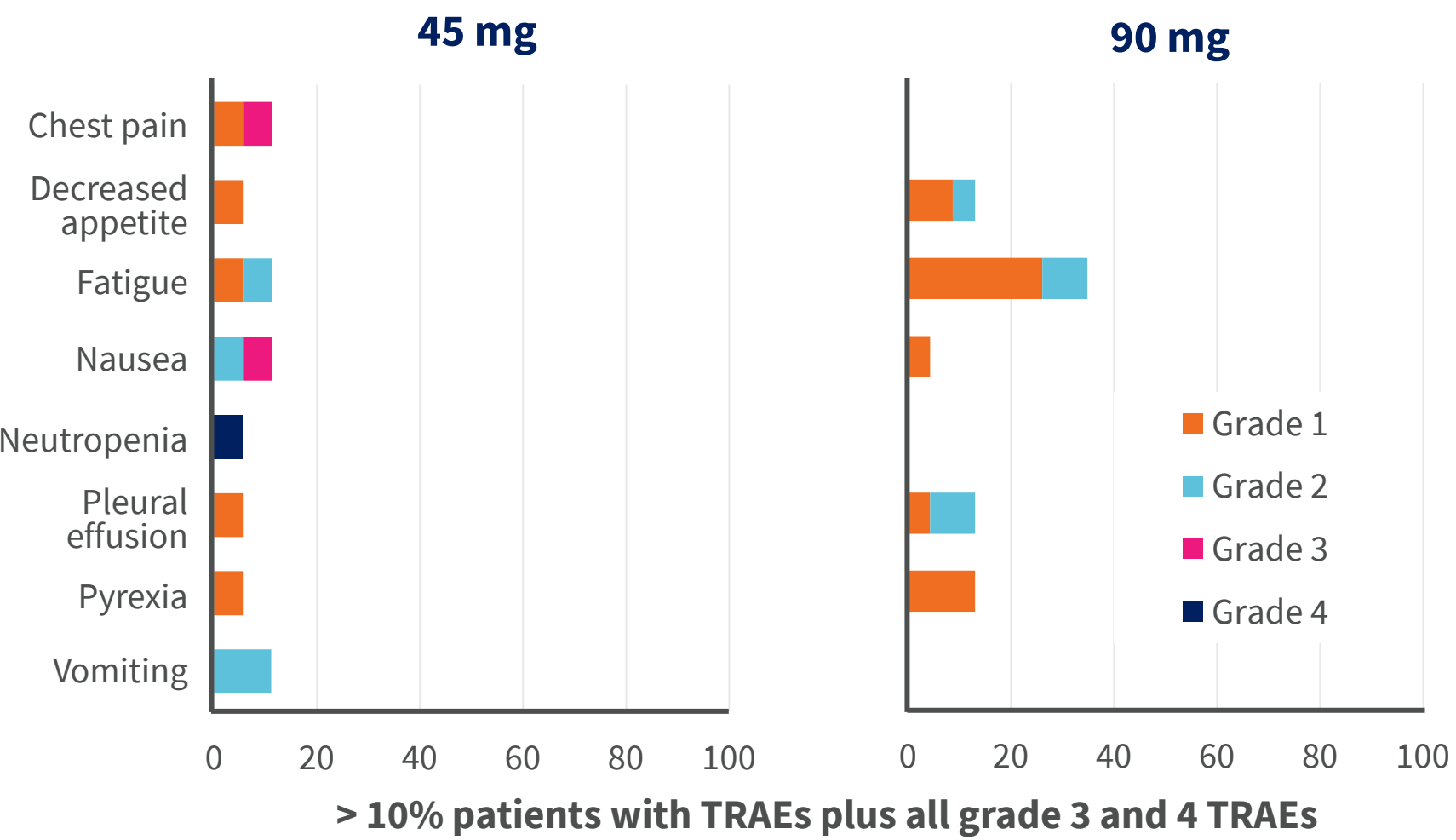
	45 mg N = 18	90 mg N = 23	Overall N = 41
Median age (years)	73.5	74.0	74.0
Female n (%)	6 (33.3)	4 (17.4)	10 (24.0)
Male n (%)	12 (66.7)	19 (82.6)	31 (75.6)
ECOG 0 n (%)	6 (33.3)	2 (8.7)	8 (19.5)
ECOG 1 n (%)	12 (66.7)	21 (91.3)	33 (80.5)
Any prior lines of anti-cancer therapy	7* (38.9)	10 (43.5)	17 (41.5)
Any prior lines of radiotherapy	4 (22.2)	1 (4.3)	5 (12.2)
Primary malignancy			
Mesothelioma n (%)	16 (88.8)	21 (91.3)	37 (90.2)
Breast n (%)	1 (5.6)	0	1 (2.4)
Gastroesophageal junction n (%)	0	1 (4.3)	1 (2.4)
Lung n (%)	1 (5.6)	1 (4.3)	2 (4.9)

*One patient had received letrozole for breast cancer.

Both doses were equally well tolerated

- Most common TEAEs ≥ grade 3: catheter site infection, dyspnea, pneumonia
- Localized reactions managed symptomatically
- TRAEs in 56% patients, mostly grade 1 or 2
 - 3 grade 3 (chest pain, nausea), 1 grade 4 (neutropenia)
- No treatment-related deaths
- SAEs in 61% and 44% of patients receiving 90 and 45 mg, respectively
 - pneumonia in 13 vs 0%

TRAEs mainly limited to grade 1 & 2



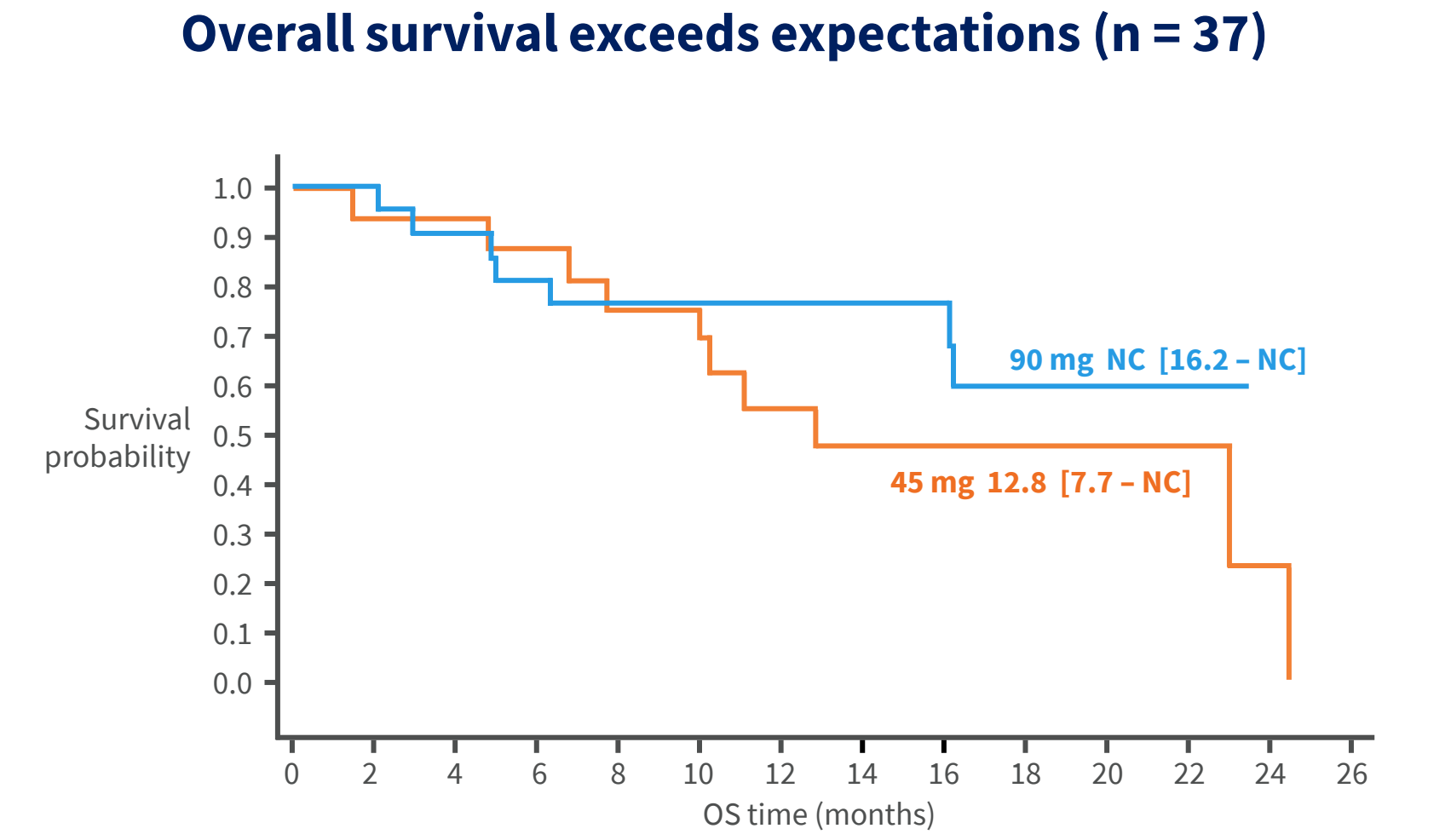
Exposure better at 90 mg

- Exposure at 90 mg substantially higher than 45 mg
 - similar relative dose intensity
 - treated for 2.6 and 1.5 months, respectively
 - cumulative doses of 630 and 270 mg, respectively

Tumour growth control supports 90 mg

Best overall response	45 mg N = 12	90 mg N = 21	Overall N = 33
CR n (%)	0	0	0
PR n (%)	1 (8.3)	1 (4.8)	2 (6.1)
SD n (%)	8 (66.7)	13 (61.9)	21 (63.6)
PD n (%)	3 (25.0)	7 (33.3)	10 (30.3)
Objective response (CR+PR) n (%)	1 (8.3)	1 (4.8)	2 (6.1)
Disease control (SD+CR+PR) n (%)	5 (41.7)	11 (52.4)	16 (48.5)

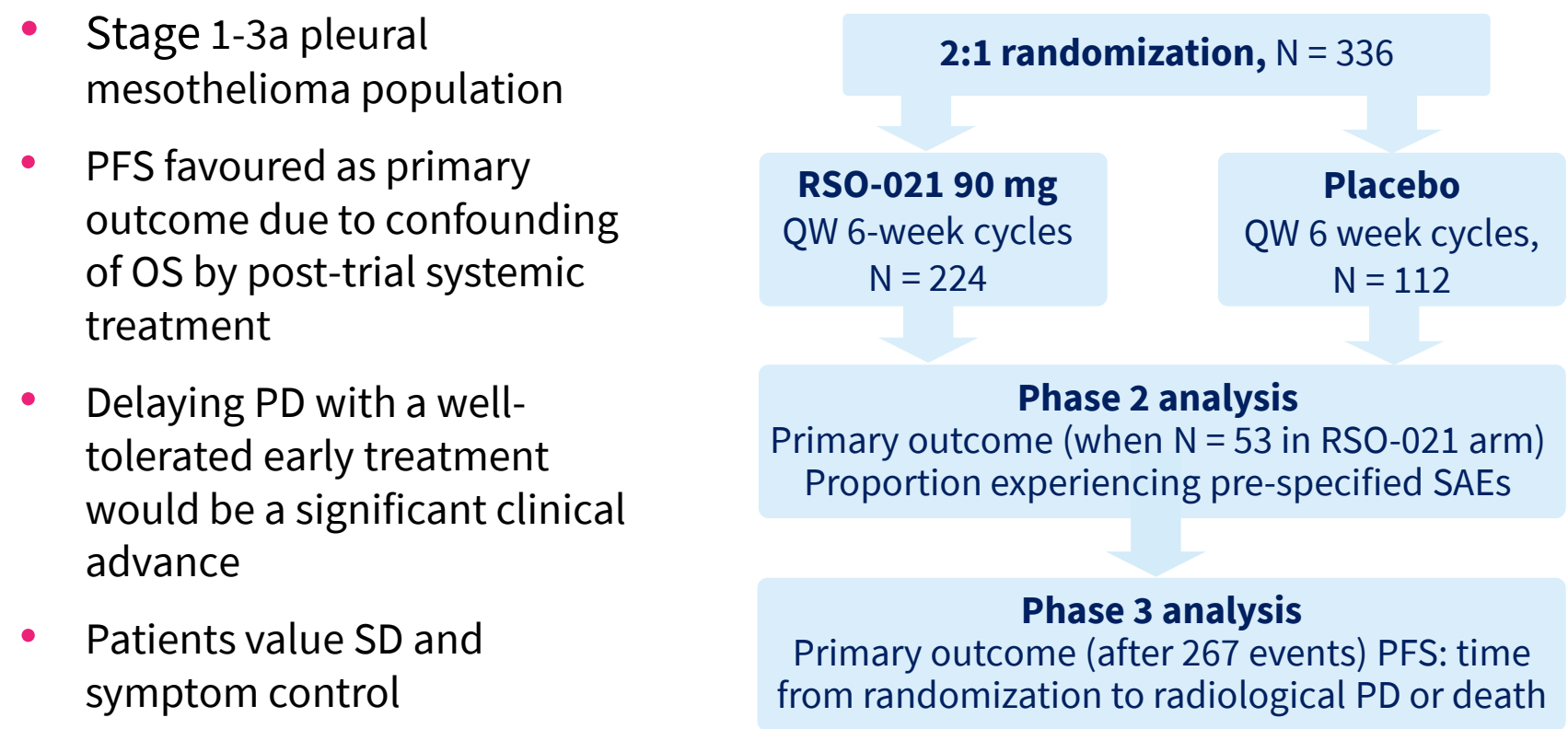
Encouraging efficacy at 90 mg



Conclusion: 90 mg for phase 3

- RSO-021 90 mg selected for phase 3 because:
 - Safety for 45 mg and 90 mg was comparable
 - 90 mg had substantially higher dose intensity
 - Efficacy outcomes (OS and DCR) favored 90 mg

Phase 3 study to address unmet need



S Dulloo disclosures: Speaker Bureau: AstraZeneca, Amgen, Roche, Regeneron, RS Oncology, Accord, Advanced Accelerator Applications (Novartis), Servier, Johnson & Johnson, Bristol Myers Squibb. Advisory Board/Consultancy: AstraZeneca, Accord, Roche, RS Oncology, Taiho, BioNTech, Boehringer Ingelheim. **Abbreviations:** CR = complete response; DCR = disease control rate; DLT = dose-limiting toxicity; ECOG = Eastern College Oncology Group; IPC = intrapleural catheter; OR = objective response; OS = overall response; PD = progressive disease; PFS = progression-free survival; PK = pharmacokinetic; PR = partial response; QW = weekly; ROS = reactive oxygen species; SAE = serious adverse event; SD = stable disease; TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event.