Phase Ib INEOV neoadjuvant trial of durvalumab +/- tremelimumab with platinum chemotherapy for patients (pts) with unresectable ovarian cancer(OC): final complete resection and pathological response rates

Authors: Alexandra LEARY[1], Thibault DE LA MOTTE ROUGE[2], Alain LORTHOLARY[3], Bernard ASSELAIN[4], Jérôme ALEXANDRE[5], Anne FLOQUET[6], Aude-Marie SAVOYE[7], Nicolas DELANOY[8], Céline GAVOILLE[9], Benoît YOU[10], Véronique D'HONDT[11], Julien GRENIER[12], Catherine GENESTIE[1], Laure CHARDIN[1], Eric-PUJADE-LAURAINE[4]

Affiliations; 1. alexandra.leary@gustaveroussy.fr - Gustave Roussy, Gynécologie Médicale, INSERM U981 VILLEJUIF CEDEX – France; 2. Centre Eugène Marquis 2 Rue de la Bataille Flandres - Dunkerque, 35042 RENNES – France; 3. Hôpital Privé du Confluent, 2 Rue Eric Tabarly 44202 NANTES – France; 4. ARCAGY-GINECO, 8 Rue Lamennais, 75008 PARIS – France; 5. Hôpital Cochin, Unité d'Oncologie Médicale, 123 Boulevard de Port-Royal - Bâtiment Copernic 75014 PARIS CEDEX 14 - France; 6. Institut Bergonié, Oncologie, 229 Cours de l'Argonne 33076 BORDEAUX CEDEX - France ; 7. Institut Jean Godinot, 1 Avenue du Général Koenig - BP 171 51056 REIMS – France; 8. Hôpital Européen Georges Pompidou, 20 Rue Leblanc 75015 PARIS – France; 9. ICL - Centre Alexis Vautrin, Avenue de Bourgogne 54519 VANDOEUVRE LES NANCY – France; 10. HCL - Centre Hospitalier Lyon Sud, Chemin Grand Revoyet - Pavillon 3F 69495 PIERRE-BENITE – France; 11. ICM, MONTPELLIER Parc Euromédecine - 208 Rue des Apothicaires 34298 – France; 12. Institut du cancer Avignon-Provence, 250 chemin de Baigne Pieds 84000 AVIGNON – France

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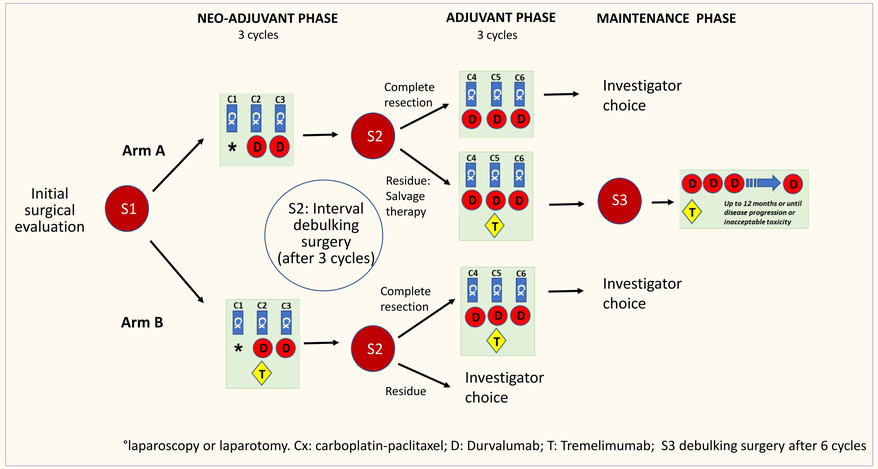
INTRODUCTION / BACKGROUND

- We have shown that neoadjuvant carboplatin and paclitaxel (NACP) increased tumor infiltrating lymphocytes and PDL1 expression in OC pts. INEOV evaluated NACP with durvalumab (D) +/- tremelimumab (T) in pts with unresectable OC. We previously reported that NACP with D+/-T was feasible and safe but the addition of T did not improve interval debulking surgery (IDS) rates after 3 cycles (C3) (ESMO 2021). Here we provide an update with longer follow up including data on delayed IDS performed after 6 cycles of neoadjuvant treatment.
- **AIMS: Describe complete resection (CC0) and complete pathological response (pCR) rates after neoadjuvant chemotherapy with D+/-T in patients with unresectable OC.**

METHODOLOGY

- Pts with stage IIIC/IV OC were randomized to NACP + D (1125mg) alone (arm A) or with T (75mg once at C2) (arm B).
- Interval debulking surgery (IDS) was planned after C3, or delayed after C6.
- Pts in arm A not operable after C3 crossed over to arm B, pts in arm B crossed over to standard of care (SOC). Pts were assessed for delayed IDS after C6.
- Macroscopic complete resection (CC0) was defined as no visible residual disease at IDS after C3 or C6 of neoadjuvant treatment.
- Complete pathological response (pCR) was defined as no residual tumor cells found on any surgical specimens, or no residual tumor cells on any samples outside the ovary at IDS.

Figure 1: INEOV trial Design



°laparoscopy or laparotomy. Cx: carboplatin-paclitaxel; D: Durvalumab; T: Tremelimumab; S3 debulking surgery after 6 cycles

KEYS CONCLUSIONS

We have shown that in patients with unresectable OC neoadjuvant CP with D+/- T results in encouraging CC0 (70%) and pCR (18%) rates. However there was no apparent benefit to the addition of T to D. Studies are ongoing to describe the immune features predictive of pCR as well as the impact of treatment on the immune microenvironment.

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RESULTS

Table 1 : Interval debulking surgery (IDS), macroscopic complete resection (CC0) and complete pathologic response (pCR) rates after neoadjuvant CP with durvalumab alone (arm A) or in combination with tremelimumab (arm B)

	Arm A (n=32)	Arm B (n=32)	All patients (n=64)
IDS performed after C3 or C6 NACT. % (N)	**81%** (26/32)	**75%** 24/32	**78%** 50/64
Macroscopic complete resection (CC0). % (N)	**75%** (24/32)	**65%** (21/32)	**70%** (45/64)
Complete pathological response evaluable only for pts who underwent IDS. % (N)	**19%** (5/26)	**16%** (4/24)	**18%** (9/50)

- Sixty four (N=64) of 66 randomized pts (IIIC/IV: 70%/30%) were evaluable.
- After C3, 66% (21/32) of pts in arm A and 59% (19/32) in arm B had IDS.
- The 11 pts in arm A not candidate for IDS after C3 crossed over to arm B until C6 and 5/11 benefited from delayed IDS.
- The 13 pts in arm B inoperable at C3 went on to receive SOC (NACP +/- bevacizumab), and 5/13 became eligible for delayed IDS after C6.
- Overall, IDS was performed in 50 of 64 evaluable pts, and most (45/50) achieved macroscopically complete resection (CC0), so that the overall CC0 rate was 70% (45/64), with no significant difference between arms (CC0= 75% vs 65% in arm A vs B).
- Among the 50 pts who had IDS, complete pathological responses were observed in 18% of pts.

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