Abstract CTIM-15

EO2401 peptide immunotherapy + nivolumab +/- bevacizumab in first recurrent glioblastoma: treatment strategy optimization in the phase 1/2 study EOGBM1-18 / ROSALIE (NCT04116658)

Society for Neuro-Oncology (SNO) / World Federation of Neuro-Oncology Societies (WFNOS) Meeting | November 19 - 23, 2025, Honolulu, HI, USA
Poster Session: Friday, November 21, 11:30am-12:45pm | Location: Hawaii Convention Center, Kamehameha Exhibit Hall II & III

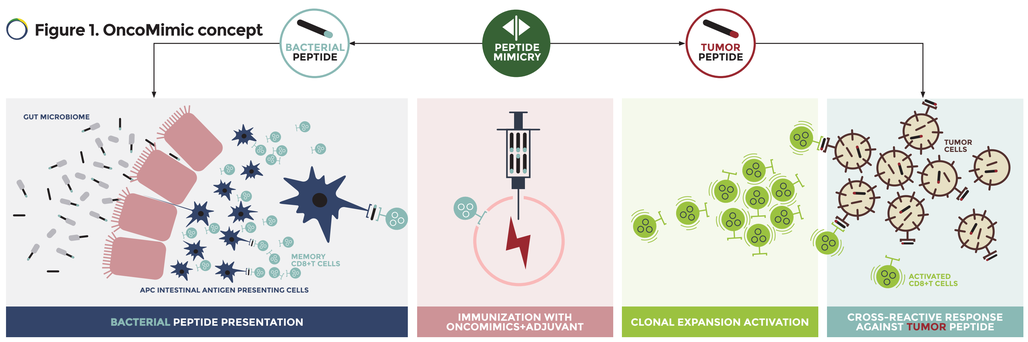
Authors: David A. Reardon[1], Ahmed Idbaih[2], Maria Vieito[3], François Ghiringhelli[4], Agostina Stradella[5], Ghazaleh Tabatabai[6], Michael C. Burger[7], Iris Mildenberger[8], Ulrich Herrlinger[9], Patrick Y. Wen[1], Mehdi Touat[2], Antje Wick[10], Macarena González[3], Alice Hervieu[4], Marta Gil-Martin[5], Mirjam Renovanz[6], Cécile Gouttefangeas[11], Ana Maia[11], Laurent Chêne[12], Jan Fagerberg[12], Philippe Rinaudo[12] , Wolfgang Wick[10]

1 Dana-Farber Cancer Institute, Boston, MA, USA; **2** Sorbonne Université, AP-HP, ICM, Hôpital Universitaire La Pitié-Salpêtrière, Paris, France; **3** Hospital Universitari Vall d›Hebron, Barcelona, Spain; **4** Centre Georges-François Leclerc, Dijon, France; **5** Institut Catala D'Oncologia - Hospital Duran i Reynals, Barcelona, Spain; **6** Universitätsklinikum Tübingen and Hertie Institute for Clinical Brain Research, Tübingen, Germany; **7** Universitätsklinikum Frankfurt Goethe-Universität, Frankfurt, Germany; **8** Medizinische Fakultät Mannheim, Mannheim, Germany; **9** Universitätsklinikum Bonn, Bonn, Germany; **10** Universitätsklinikum Heidelberg, Heidelberg, Germany; **11** Institute for Immunology, Eberhard-Karls-University Tübingen, Tübingen, Germany; **12** Enterome, Paris, France

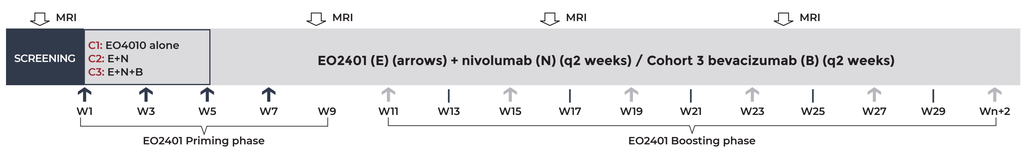
BACKGROUND

EO2401 including three HLA-A2 synthetically produced short non-self-peptide sequences from gut-bacteria (EO2316, EO2317, and EO2318) is designed to expand pre-existing memory CD8 T-cells which by peptide molecular mimicry cross-react with glioblastoma tumor associated antigens (TAAs; IL13Rα2, BIRC5/survivin, and FOXM1). A universal CD4 helper epitope, UCP2 derived from hTERT, is also included.

Figure 1. OncoMimic concept



METHODS



EO2401 in combination with nivolumab +/- bevacizumab

- **nivolumab:** support fast and extensive T cell expansion and T cell infiltration of tumor
- **bevacizumab:** anti-edema properties, counteract immunosuppression by VEGF

Endpoints

- Safety and tolerability
- Immunogenicity, clinical efficacy, extensive exploratory endpoints

Cohort 1a
EO2401 → EO2401 / nivolumab:
Measurable disease
Study part 1, n=3
Study part 2, sLDB**, n=18
Pts part 1 = safety lead-in

Cohort 2a
EO2401 / nivolumab:
Measurable disease
Study part 1, n=23
Study part 2, sLDB**, n=15

Cohort 2b
EO2401 / nivolumab:
Non-measurable^ disease (intended adjuvant)
Study part 1, n=3
Study part 2, sLDB**, n=3

Cohort 2c
EO2401 / nivolumab:
Measurable disease
Peri-operative treatment
Study part 2, sLDB**, n=9

Cohort 3
EO2401 / nivolumab / bevacizumab*:
Measurable disease
Study part 1+2, n=26

EOGBM1-18
EO2401 / nivolumab +/- bevacizumab
Total study n=100

EO2401:
300µg/peptide, every 2 weeks x 4, then every 4 weeks; administered SC with adjuvant Montanide ISA 51 VG

nivolumab:
3 mg/kg every 2 weeks (Cohort 1 start week 5, other Cohorts start week 1)

bevacizumab:
* Standard dose (Cohort 3) = 10 mg/kg every 2 weeks start week 1, until PD
** Possible symptomatic low dose (sLDB) = 5 mg/kg every 2 weeks start at neurological symptoms

^Non-measurable enhancing disease (<1x1 cm in maximum bi-perpendicular plane)

The current presentation focuses on Cohort 2a/2b (n=44; 6 pts receiving sLDB) and Cohort 3 (n=26)

Patients: first recurrent glioblastoma, HLA-A2 positve (EO2401 specificity), KPS >= 70, no dexamethsone >2mg/day within 14 days before EO2401.

BASELINE CHARACTERISTICS

E = EO2401 N = NIVOLUMAB * 6 pts <100 mm2 B = BEVACIZUMAB DB 2024-03-04 (FINAL)	Cohort 2a/2b EN (n=44*)	Cohort 3 ENB (n=26)
Age; median (range), years	58.0 (18-78)	60.5 (24-73)
Gender; % female - %male	41% - 60%	38% - 62%
Time from initial diagnosis to study start; median (range), months	12.4 (6.0-54.5)	10.7 (6.6-97.5)
MGMT promoter methylation; % yes - % no	34% - 66%	36% - 64%
IDH1 mutation; # (%)	2 (5%)	3 (12%)
Baseline target lesion size; median (range), mm²	644 (0-4290)	1061 (110-3930)
Baseline KPS (%); % ≥ 90 - % 70 to 80	52% - 48%	54% - 46%
Baseline steroid use; % yes (DEX ≤ 2 mg per eligibility)	34%	31%
2nd surgery (within 101 days of start EO2401) for recurrent disease before EN/ENB start; % yes	23%	31%

EFFICACY

E = EO2401 N = NIVOLUMAB * C2b non-measurable disease at baseline. NA = not available; NE = not estimable NOTE, all time estimates from start of EO2401 B = BEVACIZUMAB DB 2024-03-04 (FINAL)	Cohort 2a/2b EN (n=44)	Cohort 3 ENB (n=26)
Treatment duration; median (range), months	2.31 (0.03-20.14)	4.75 (0.53-20.11)
Objective response rate	NA*	38%
Duration of confirmed response; median (95% CIs), months	NA*	7.4 (3.7-16.7)
Disease control rate	36%	88%
Duration of disease control; median (95% CIs), months	8.2 (5.3-11.1)	5.5 (3.7-7.4)
Progression-free survival; median (95% CIs), months	1.9 (1.7-2.8)	4.8 (3.7-7.3)
Follow-up for survival; median, months	25.0	33.6
Survival; median (95% CIs), months	10.8 (6.3-14.3)	12.1 (8.0-14.8)
Survival rates (KM-estimates) 6-months 12-months 18-months 24-months	73.7% 45.5% 20.5% 11.4%	84.6% 53.8% 26.4% 10.5%

COX REGRESSION ANALYSES FOR SURVIVAL OUTCOMES

METHODS

Multivariable Cox regression analyses including age, sex, MGMT-methylation-status, baseline target tumor size (log-transformed), baseline corticosteroid use, and secondary surgery (≤101 days before EO2401-start) were applied. An iterative forward–backward stepwise selection procedure identified independent predictors of overall survival. Non-retained covariates are shown as univariate Cox results.

RESULTS

- **Cohort 2a/2b (EO2401/nivolumab):**
  - second surgery not significant (HR 1.09; 0.43–2.75; p = not significant)
  - no covariate retained by stepwise Cox (i.e., no significant outcome for age, sex, MGMT-methylation-status, baseline target tumor size, baseline corticosteroid use, or second surgery)
- **Cohort 3 (EO2401/nivolumab/bevacizumab):**
  - second surgery favorable for survival (HR 0.08; 0.01–0.75; p = 0.027)
  - male sex (HR 10.2; 2.17–48.3; p = 0.003) and baseline corticosteroid use (HR 9.35; 2.03–43.1; p = 0.004) unfavorable for survival
  - age, MGMT-methylation-status, and baseline target tumor size not significant
- Sensitivity analysis by MGMT-methylation status imputation (all missing non-methylated, alternatively all missing methylated) had no impact on conclusions.

EXTERNAL VALIDATION OF COX REGRESSION ANALYSES FOR SURVIVAL OUTCOMES.

CheckMate-143, JAMA Oncol 2020; 6(7):1003-1010

- **bevacizumab treatment:**
  - second surgery before treatment start = no significant impact (HR 0.88; 0.47–1.65)
  - no predictors retained (see methods)
- **nivolumab treatment:**
  - second surgery before treatment start = no significant impact (HR 1.31; 0.78–2.20)
  - retained predictors with significant outcomes were MGMT-methylation-status (methylated status favorable, HR 1.95; 1.12–3.17; p = 0.007) and baseline corticosteroid use (use unfavorable, HR 2.30; 1.42–3.71; p = 0.001)
- **overall frequency of second surgery in evaluated patients:**
  - bevacizumab treated patients 37/166 (22.3%); 12 patients with 2nd surgery and all defined variables available
  - nivolumab treated patients 49/182 (26.9%); 21 patients with 2nd surgery and all defined variables available
  - rates consistent with overall and complete-covariate subsets.

Figure 3. Cohort 2a/2b: second surgery before EO2401/nivolumab no significant impact

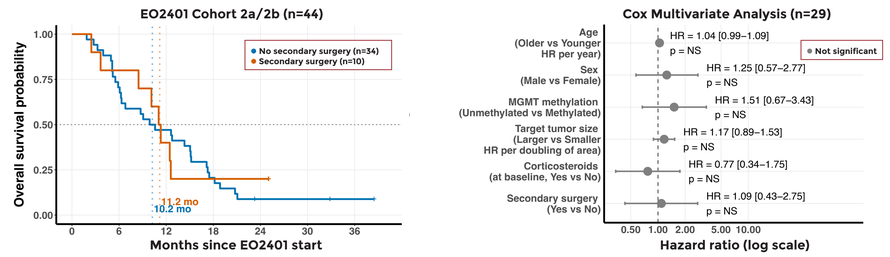


Figure 4. Cohort 3: second surgery beneficial before start EO2401/nivolumab/bevacizumab

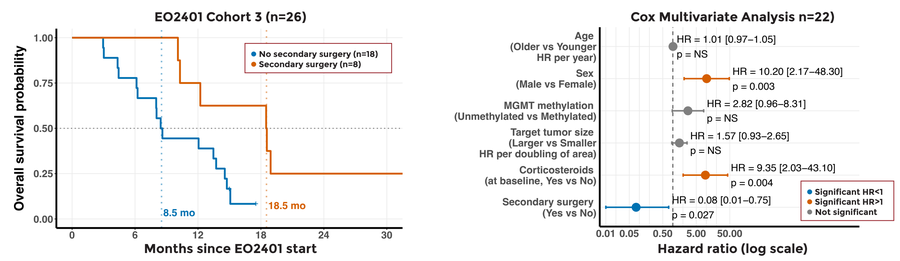


Figure 5. Cohort 2a/2b & 3: Type of second surgery outcome does NOT impact survival or tumor size at baseline before start of EO2401/nivolumab +/- bevacizumab

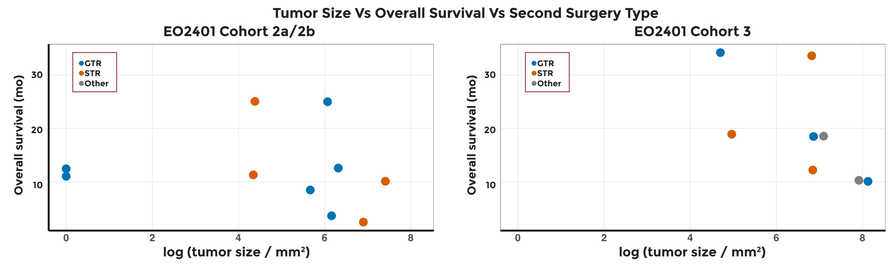


Figure 6. CheckMate-143: second surgery before bevacizumab no significant impact

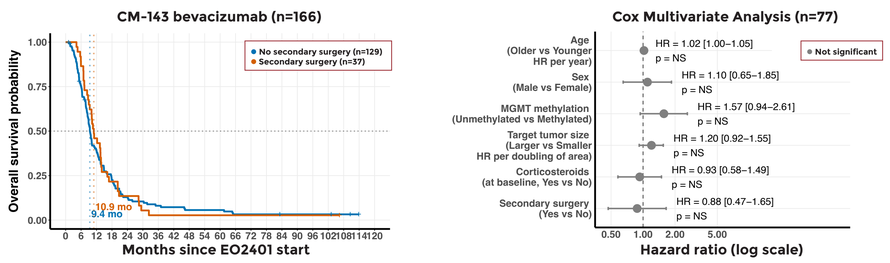
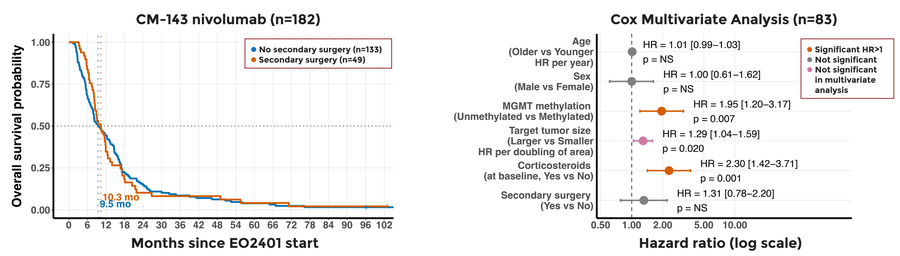


Figure 7. CheckMate-143: second surgery before nivolumab no significant impact



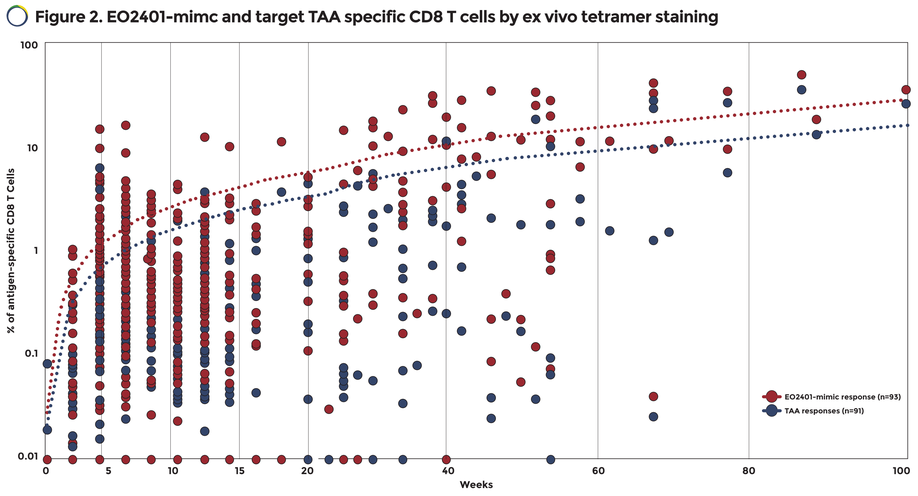
OVERALL IMMUNE RESPONSE (n=96):

EO2401-mimic specific response corresponds to the cumulative % of CD8 T cells specific for EO2316, EO2317 and EO2318; TAA-specific response corresponds to the cumulative % of CD8 T cells specific for IL13RA2, BIRC5 and FOXM1. Each dot represents a patient; values across timepoints are plotted. Dashed lines represent nonlinear fitting curves. Negative responses were set to 0.01 for logarithmic representation. Tests on cryopreserved peripheral mononuclear cells after thawing using peptide specific tetramers/flow cytometry with cells ex vivo without any in vitro stimulation.

Overall, immunomonitoring could be performed for 96 patients, and 91 demonstrated at least one positive response in either tetramer or ELISPOT assays, yielding an overall positivity rate of 95%.

Immunomonitoring demonstrated by tetramers / ex vivo expansion of CD8 T cells specific for EO2401-mimic and target TAAs in 82% / 81% of tested patients in Cohort 2a/2b and in 92% / 92% in Cohort 3.

Figure 2. EO2401-mimc and target TAA specific CD8 T cells by ex vivo tetramer staining



CONCLUSIONS

- **EO2401 / nivolumab +/- bevacizumab was well tolerated with a safety profile consistent with the safety profile of nivolumab, and when applicable the safety profile of bevacizumab, except the addition of local administration site reactions of mainly Grade 1-2 in approximately half of the patients.**
- **EO2401/nivolumab, generated fast, strong, and durable specific CD8 T cell immune responses against the EO2401-mimic peptides and target epitopes on tumor associated antigens.**
- **Addition of bevacizumab with strong anti-edema properties, and possibility to counteract immunosuppression by VEGF, to EO2401/nivolumab has increased treatment duration and efficacy.**
- **There is a further survival benefit if EO2401/nivolumab/bevacizumab is utilized as adjuvant treatment after surgery for first recurrent glioblastoma (2nd surgery).**
  - **The effect is NOT seen with either of the EO2401-supportive drugs nivolumab or bevacizumab alone. This suggests a synergistic, immune-mediated interaction supporting the integration of surgery with broader "respectability-indications" than today (since extent of resection does not seem to influence outcome, but other surgery induced effects on the tumor/environment might be at play) into the further development of EO2401.**
- **The data indicate that a randomized study evaluating EO2401 is warrented.**

Individual patient data from the CheckMate-143 study was kindly provided by Bristol Myers Squibb, Princeton, New Jersey, USA