Presentation Number 170P

EO2401 microbiome derived therapeutic vaccine + nivolumab +/- bevacizumab, in neoadjuvant, adjuvant and non-surgery linked treatment of recurrent glioblastoma: Phase 1-2 EOGBM1-18/ROSALIE Study

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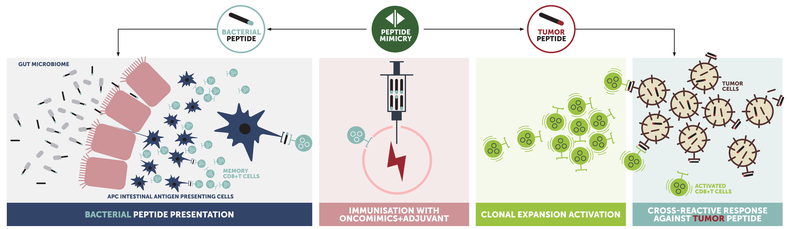
BACKGROUND

Recurrent glioblastoma (GB) has a poor prognosis and a limited number of treatment options, with an expected median survival around 8-9 months in trials with longer follow-up (Wick W, Gorlia T, Bendszus M, et al. Lomustine and bevacizumab in progressive glioblastoma (EORTC 26101). N Engl J Med. 2017;16;377(20):1954-1963). EO2401 is composed of three high-affinity microbial-derived synthetically produced peptides mimicking CD8+ T cell HLA-A2 epitopes from the tumor associated antigens IL13Rα2, BIRC5/survivin, and FOXM1, and the helper CD4+ peptide UCP2. Nivolumab supports T cell expansion and infiltration of tumor. Bevacizumab has anti-edema properties and can counteract immunosuppression by VEGF.

METHODS

This ongoing phase 1/2 trial (EOGBM1-18/ROSALIE, NCT04116658) investigates EO2401 + nivolumab +/- bevacizumab in patients with GB at first progression / recurrence after surgery and adjuvant radiotherapy / temozolomide. Patients were HLA-A2, and had KPS ≥70, ≤ dexamethasone 2 mg/day within 14 days before study, normal organ functions, no contraindications. Treatment is given until toxicity or tumor progression using the iRANO criteria.

The microbiome-mimicry concept utilizing high affinity MHC class I, non-self-microbiome-derived peptides mimicking TAAs exhibited by tumor cells to expand pre-existing memory cytotoxic T cells cross-reacting with the selected TAAs



COHORTS, TREATMENTS, AND SCHEDULES

Treatment Cohort	Study part 1	Study part 2; symptom driven low-dose bevacizumab** as time-limited anti-edema treatment	Total
Cohort 1a (E→+EN): EO2401 mono x2 (4 weeks), followed by EO2401/nivolumab (measurable disease)	3 patients	18 patients	21 patients
Cohort 2a (EN): EO2401/nivolumab (measurable disease)	23 patients	15 patients	38 patients
Cohort 2b (EN): EO2401/nivolumab adjuvant after surgery for recurrence (non-measurable disease)	3 patients	3 patients	6 patients^
Cohort 2c (EN): EO2401/nivolumab neoadjuvant and adjuvant in relation to surgery for recurrence	N/A	8 patients	8 patients
Cohort 3 (ENB): EO2401/nivolumab/bevacizumab* (measurable disease)	11 patients	N/A	11 patients

EO2401: 300 µg/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 **** Low dose** = 5 mg/kg every 2 weeks start at neurological symptoms ^ Two patients non-evaluable due to no surgery for recurrent disease

BASELINE CHARACTERISTICS

Baseline Characteristics	Cohort 1a E→EN (n=21)	Cohort 2a EN (n=38)	Cohort 2b EN adjuvant (n=6)	Cohort 3 ENB (n=11)	Total Cohorts 1a, 2a, 2b, 3 (n=76)	Cohort 2c EN neoadjuvant → surgery → adjuvant (n=8)
Age, median (range), years	58.0 (19-73)	59.0 (18-78)	53.5 (46-70)	64.0 (24-72)	**58.5 (18-78)**	53.0 (41-67)
Gender, female/male	33% / 67%	40% / 60%	50% / 50%	64% / 36%	**42% / 58%**	38% / 62%
KPS ≥ 90% (Yes/No)	67% / 33%	39% / 61%	83% / 17%	36% / 64%	**50% / 50%**	100% / 0%
MGMT promoter methylation (Yes/No)	35% / 65%	36% / 64%	40% / 60%	80% / 20%	**43% / 57%**	43% / 57%
IDH1 mutation (Yes)	0	1 (3%)	1 (17%)	2 (18%)	**4 (5%)**	1 (13%)
Baseline steroid use (0 < dexamethasone ≤ 2 mg)	23%	34%	50%	36%	**33%**	0%
Time from initial diagnosis of glioblastoma to study treatment start, median (range), months	12.6 (6.3-38.3)	12.0 (6.0-54.5)	13.25 (6.0-36.0)	7.7 (0.7-96.6)	**12.2 (0.7-96.6)**	14.6 (5.2-58.5)

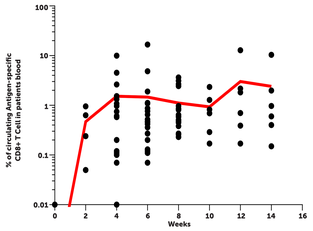
SAFETY (DB 2022-06-23; n =76 from Cohorts 1a, 2a, 2b, and 3)

EO2401 + nivolumab +/- bevacizumab safety profile consistent with the profile of nivolumab, and when applicable bevacizumab, except the addition of local administration site reactions

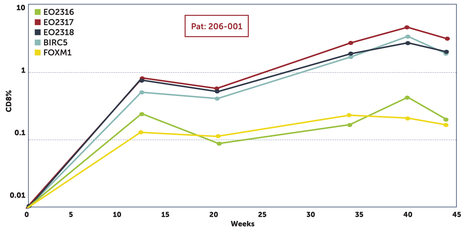
- Grade 3/4 related events in 17% of patients
- Most common treatment-related AEs were fatigue (22%), injection site reaction (16%), and ALT increase (11%)
- Five AEs leading to treatment discontinuation: transaminitis (2), aseptic meningitis, newly diagnosed CRC, alteration general status
- Immune mediated AEs necessitating action: transaminitis (2), hypothyroidism (2), aseptic meningitis (2), rash (2)
- Any local administration site event (main erythema, induration, pain) in 45% of patients:
  - severity of events 70% Grade 1, 26% Grade 2, and 4% Grade 3
  - median time to event onset 38 days (range 1-446)
  - KM analysis median event duration 28 days

IMMUNE RESPONSE

Fast, strong, and durable memory CD8+ T cell response with strong cross-reactivity against human TAAs



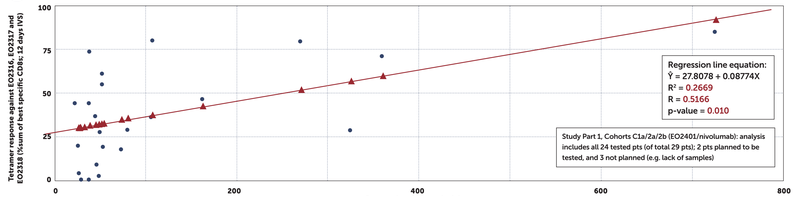
% of CD8+ T cells specific for EO2316, EO2317, and EO2318 as assessed with tetramer analysis ex vivo*



% of CD8+ T cells specific for EO2316, EO2317, EO2318, and the human TAAs BIRC5 and FOXM1 as assessed with tetramer analysis ex vivo*

* ex vivo assay: PBMC separated from peripheral blood directly analyzed by flow cytometry of CD8+ cells using specific tetramers staining without any prior in vitro stimulation

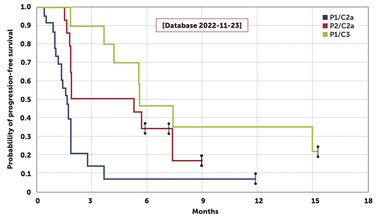
Strength of immune response direct correlating with clinical outcome [Database 2022-11-23]



EO2401 treatment duration, ORR, and PFS; impact of bevacizumab

E = EO2401 N = nivolumab B = bevacizumab	Study Part 1 Cohort 2a (n=23) EN (no B)	Study Part 2 Cohort 2a (n=15) EN + symp. LDB*	Study Part 1 Cohort 3 (n=11) ENB**
median treatment duration (95% CI)	1.4 months (95% CI 0.9; 2.3)	3.2 months (95% CI 1.1; 8.3)	5.0 months (95% CI 2.3; 14.5)
objective response rate (95% CI)	8.7% (95% CI 1.1; 28.0)	20.0% (95% CI 4.3; 48.1)	54.5% (95% CI 23.4; 83.3)
median PFS (95% CI)	1.6 months (95% CI 1.1; 1.8)	3.6 months (95% CI 1.8; 7.4)	5.5 months (95% CI 1.8; 15.2)
pts on study treatment	0 (0%)	3 (20%)	1 (9%)

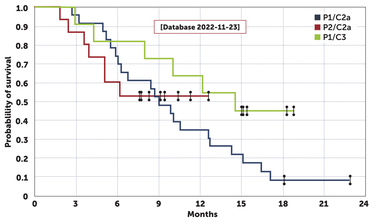
* symptom driven low-dose bevacizumab as time-limited anti-edema treatment, median 3 administrations, was given to 5 (33%) patients in Cohort 2a
** standard US PI continuous dose bevacizumab



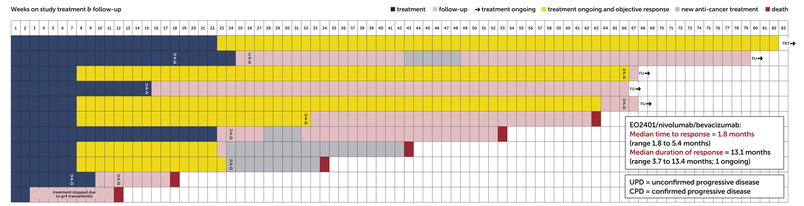
EO2401 overall survival; impact of bevacizumab

	Study Part 1 Cohort 2a (n=23) EN (no B)	Study Part 2 Cohort 2a (n=15) EN + symp. LDB*	Study Part 1 Cohort 3 (n=11) ENB**
median follow-up for survival	20.5 months	9.3 months	15.4 months
median survival (95% CI)	9.0 months (95% CI 6.1; 12.6)	not reached (95% CI 3.6; ne)	14.5 months (95% CI 4.3; ne)
pts alive	2 (9%)	8 (53%)	5 (45%)

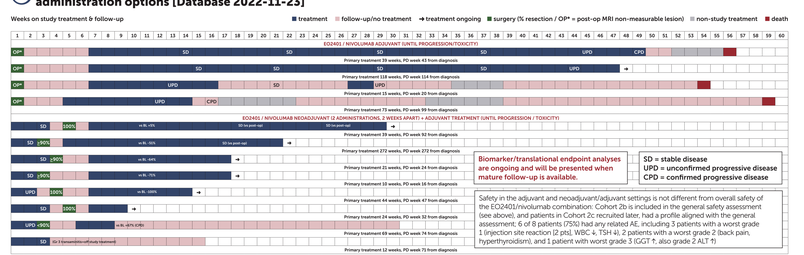
* symptom driven low-dose bevacizumab as time-limited anti-edema treatment, median 3 administrations, was given to 5 (33%) patients in Cohort 2a
** standard US PI continuous dose bevacizumab



Long response durations for the ENB triplet; EO2401 + nivolumab + bevacizumab (Cohort 3) [Database 2022-11-23]



Adjuvant (Cohort 2b) and neoadjuvant/adjuvant (Cohort 2c) EO2401/nivolumab are clinically feasible administration options [Database 2022-11-23]



CONCLUSIONS

- EO2401/nivolumab +/- bevacizumab was well tolerated with a safety profile consistent with the safety profiles of nivolumab and bevacizumab, except the addition of local administration site reactions
- EO2401/nivolumab generated fast, strong, and durable memory CD8+ T cell immune responses correlating with efficacy
- Adjuvant and neoadjuvant/adjuvant administration of EO2401/nivolumab are clinically feasible administration options
- Symptom driven use of low-dose, time-limited, bevacizumab supported longer treatment durations of EO2401/nivolumab, and some improvement of efficacy
- Addition of standard bevacizumab to EO2401/nivolumab improved efficacy
- Additional patients are treated with "the triplet" EO2401/nivolumab/ bevacizumab (ENB) to support final regimen selection for further studies

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