16th CONGRESS Lung ON CANCER

BARCELONA 27 / 28 NOVEMBER 2025

GECP lung cancer research

Other immunotherapy strategies: Vaccines, oncolytic virus, cellular therapy

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Enriqueta Felip, declaration of interests

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Potential therapeutic approaches to overcome immune checkpoint inhibitor resistance

ENHANCE TUMOR IMMUNOGENICITY	ENHANCE T-CELL FUNCTION AND INFILTRATION	TARGET IMMUNE SUPPRESSIVE TME
Combination with chemo / ADC/ RT	Combination with other CPIs, e.g. LAG3 or TIGIT	Combination with anti-angiogenics
Vaccines/ oncolytic viruses	Cellular therapies, e.g. CAR-T cells, TILs	Combination with TAM receptor inhibitors
Other targeted therapies	TLR9 / STING agonists, HDAC inhibitors T/NK cell engagers	Adenosine pathway inhibitors
Combination with DNA damage repair inhibitors	Co-stimulatory signals (e.g. OX40, cytokines e.g. IL-2)	Targeting Tregs & MDSCs

Aldea Cancer Discov (2021); Mamdani Front Immunol (2022); Horvath Mol Cancer (2020); Frisone Front Oncol (2022); Wang Front Oncol (2020)

Courtesy Dr Solange Peters

Cancer vaccines

Prophylactic cancer vaccines

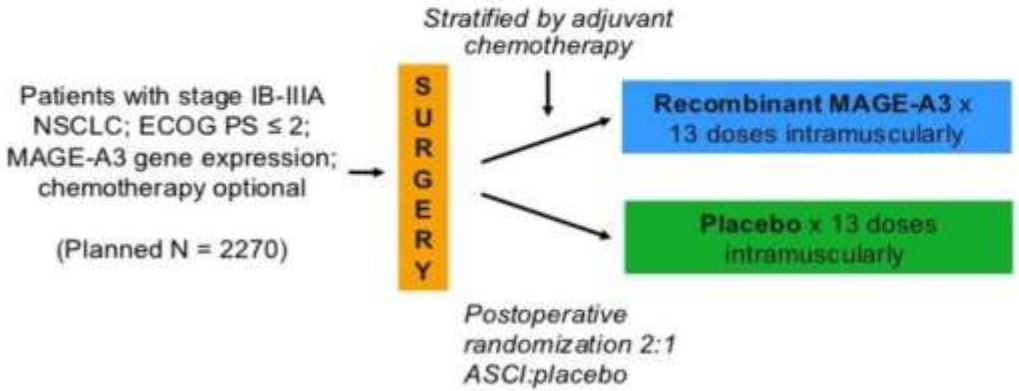
- Aimed at preventing cancer from developing
- Generally target agents that cause or contribute to cancer development

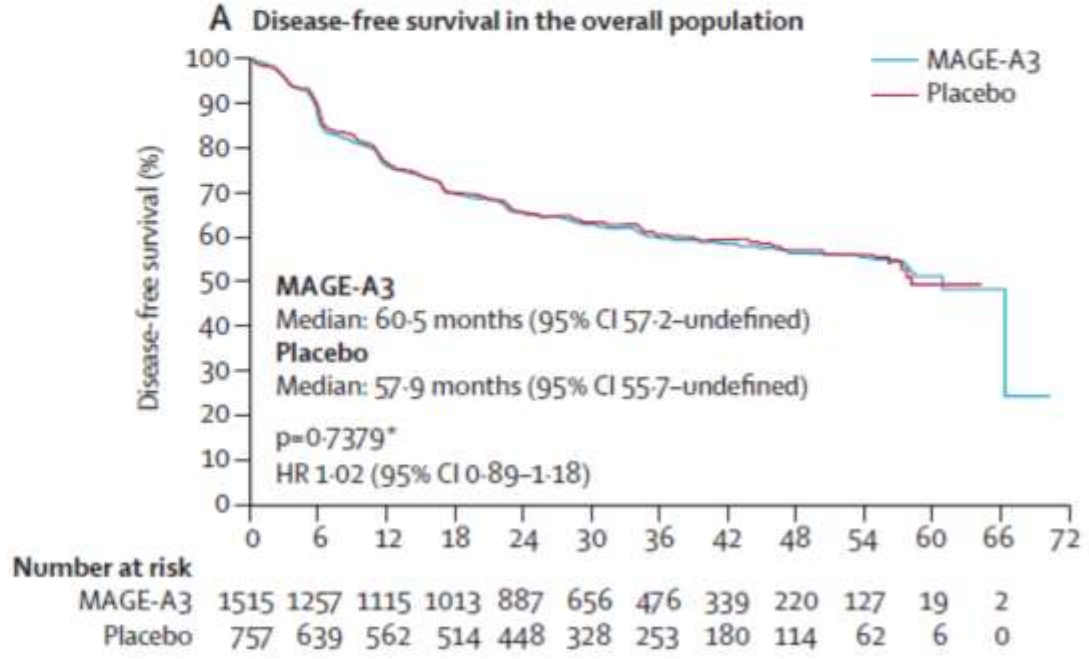
Therapeutic cancer vaccines

- Designed to treat cancers that have already developed
- Target tumor-associated antigens or tumor-specific antigens

Vaccines Against Tumor Associated Antigens

MAGRIT: MAGE-A3 Vaccine





Vansteenkiste Lancet Oncol 2016

Randomized open-label controlled study of cancer vaccine OSE2101 versus chemotherapy in HLA-A2-positive patients with advanced non-small-cell lung cancer with resistance to immunotherapy: ATALANTE-1☆

B. Besse[1,*], E. Felip[2], R. Garcia Campelo[3], M. Cobo[4], C. Mascaux[5], A. Madroszyk[6], F. Cappuzzo[7], W. Hilgers[8], G. Romano[9], F. Denis[10], S. Viteri[11], D. Debieuvre[12], D. Galetta[13], E. Baldini[14], M. Razaq[15], G. Robinet[16], M. Maio[17], A. Delmonte[18], B. Roch[19], P. Masson[20], W. Schuette[21], A. Zer[22], J. Remon[1], D. Costantini[23], B. Vasseur[23], R. Dziadziuszko[24] & G. Giaccone[25], on behalf of the ATALANTE-1 study group

2023

OSE2101 (5 TAA)[1] v doc or pem post chemo-IO, advanced non-sq NSCLC (ATALANTE-1)

[1]HER-2/neu, CEA, MAGE 2, MAGE 3 and p53

- Advanced/metastatic NSCLC
- EGFRwt, ALK-negative, all PD-L1 status
- HLA-A2+ (blood)
- Failure to platinum-based CT and IO, combined or sequenced
- IO last line with primary or secondary resistance*
- Brain metastases allowed if asymptomatic & treated
- ECOG PS 0 to 1

R 2:1

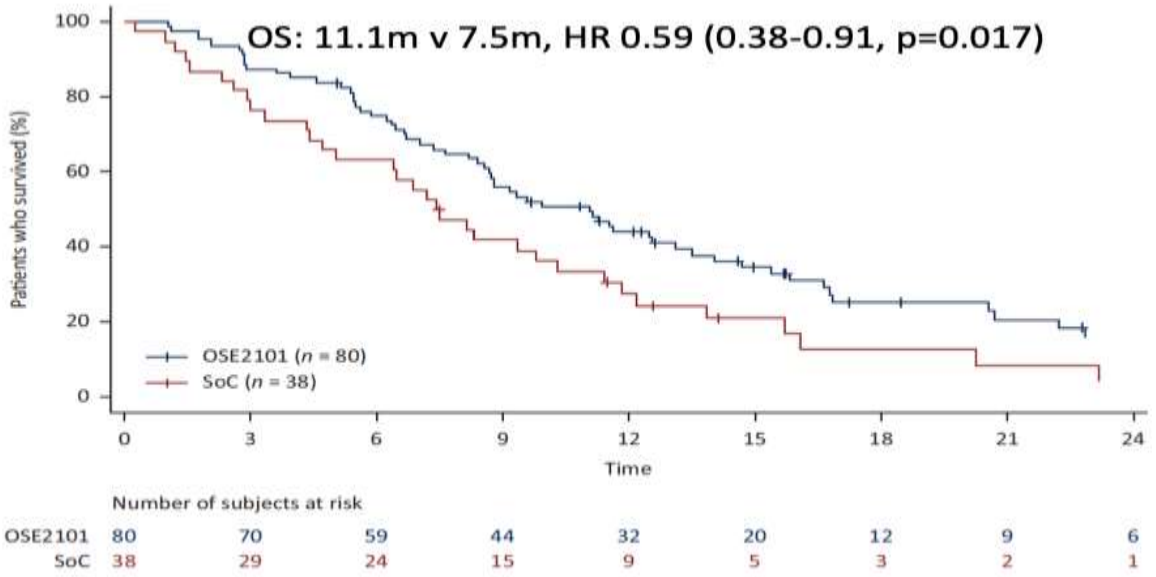
Arm A: OSE2101 Q3W for 6 subcutaneous injections, then Q8W up to Year 1, then Q12W until progression or toxicity

Arm B: SoC (docetaxel or pemetrexed) Q3W until progression or toxicity

Primary endpoint: OS

Stratification
- Histology
- Best response to 1st line
- Line rank of prior IO

*Primary resistance: failure within 12 weeks of IO, secondary resistance: failure after minimum 12 weeks of IO; Kluger *et al.*, 2020



OSE2101 is a T-specific immunotherapy designed to induce cytotoxic T lymphocytes against 5 tumor-associated antigens frequently overexpressed in NSCLC (HER-2/neu, CEA, MAGE 2, MAGE 3 and p53). This vaccine is composed of 9 synthetic peptides that are presented in lung cancer cells by the HLA-A2 phenotype (45% of the population)

KEY ELIGIBILITY CRITERIA
- HLA-A2+ (in blood by central lab)
- Metastatic squamous & non-squamous NSCLC without EGFR, ALK, ROS-1; other actionable mutations known to be immunosensitive are eligible in case of lack of local access to targeted therapy (i.e.; KRAS G12C and BRAF mutations)[1]
- Secondary resistance to immune checkpoint inhibitor defined as progressive disease (PD) after ≥ 24 weeks of first line CT-ICI, including at least 12-weeks of anti-PD(L)1 inhibitor monotherapy prior to randomisation[2]
- ECOG PS 0 to 1
- No brain metastasis or previously treated brain metastasis

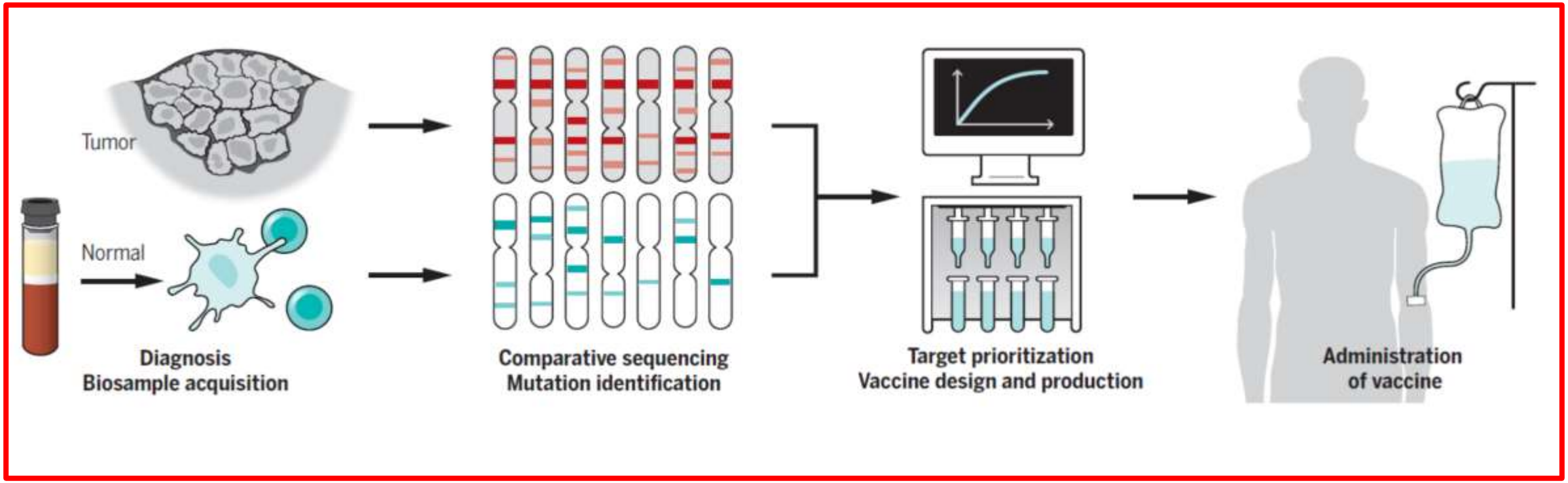
Randomisation 2:1

ARM A: OSE2101 (n=242)
Q3W for 6 subcut. inj., then Q8W until end Year 1, then Q12W Year 2[3] until PD, toxicity or consent withdrawal

ARM B: DOCETAXEL (n=121)
Q3W iv infusion until PD, toxicity or consent withdrawal

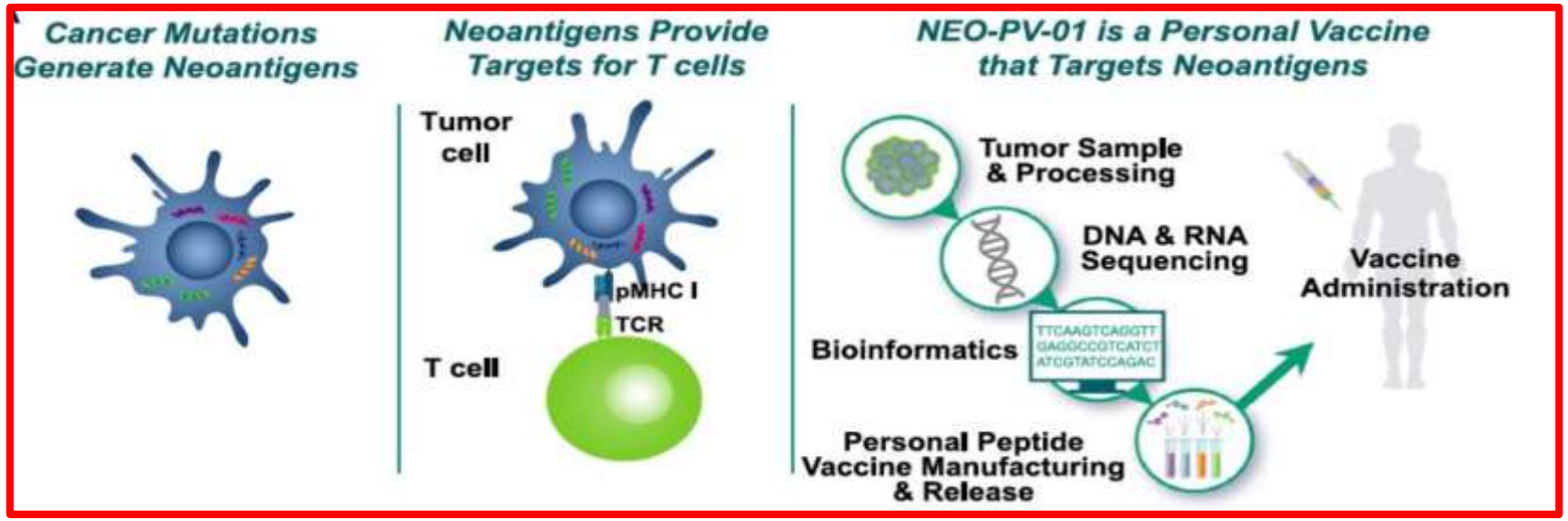
Stratification
- Histology (squamous vs non-squamous)
- ECOG PS (0 vs 1)

Personalized cancer vaccines

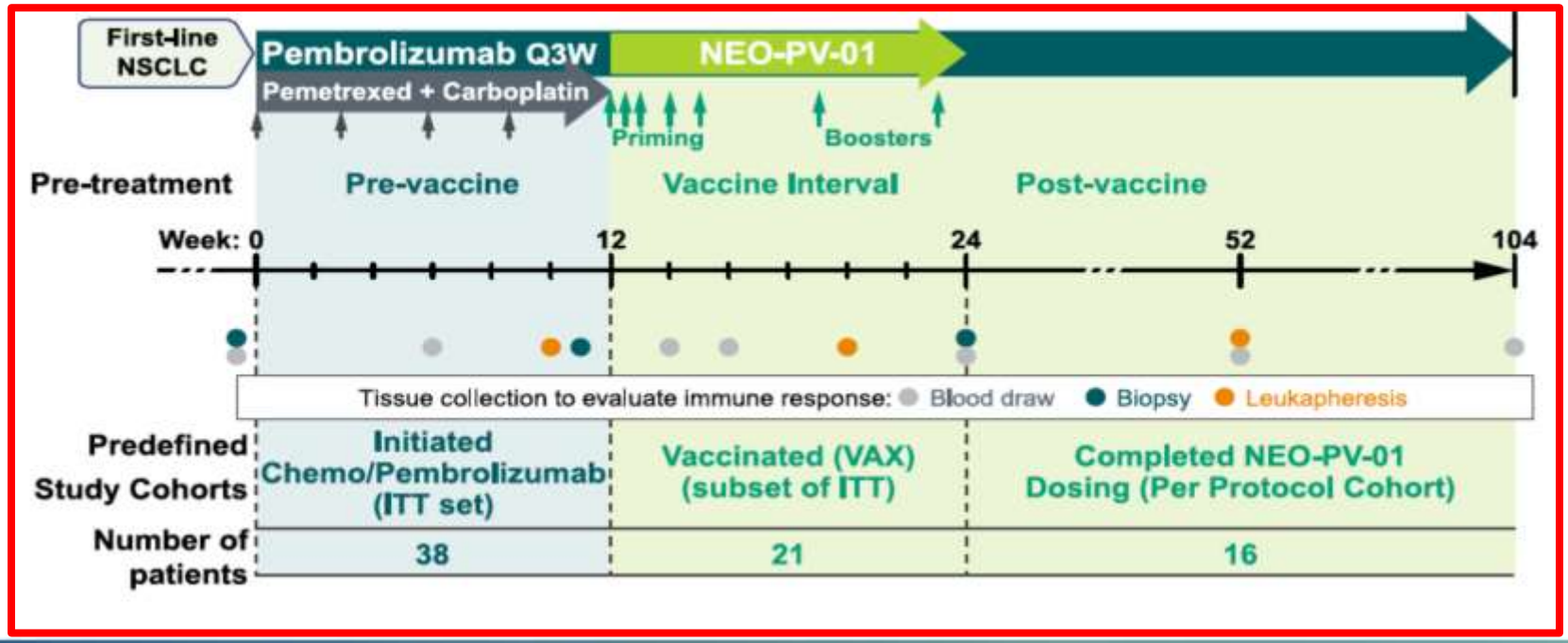


Sahin Science 2018

Personalized neoantigen vaccine NEO-PV-01 with chemotherapy and anti-PD1 as 1L treatment for non-squamous NSCLC

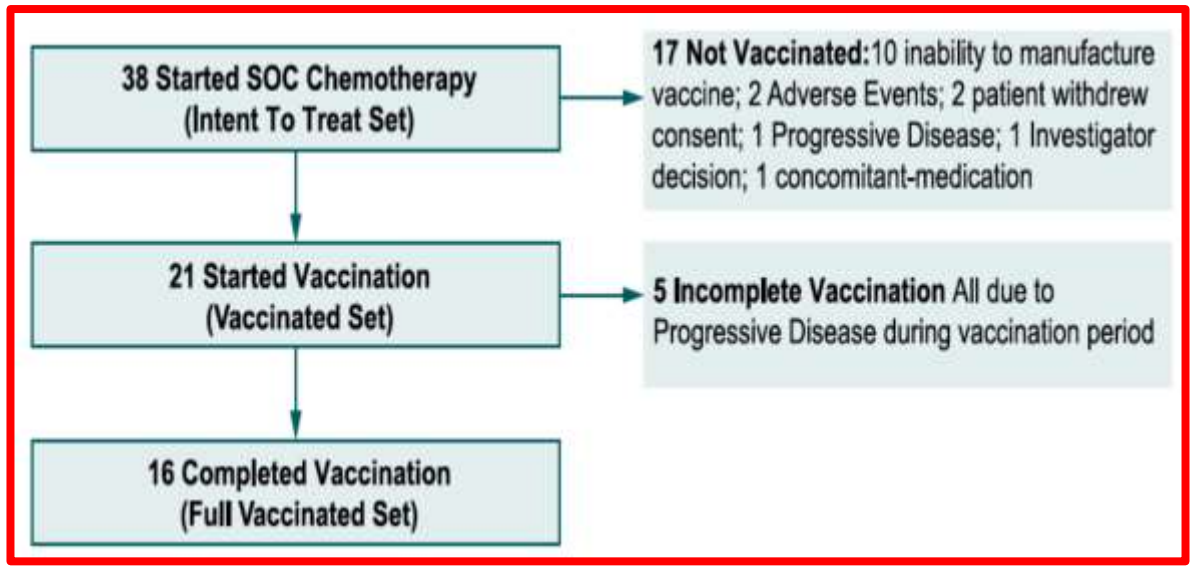


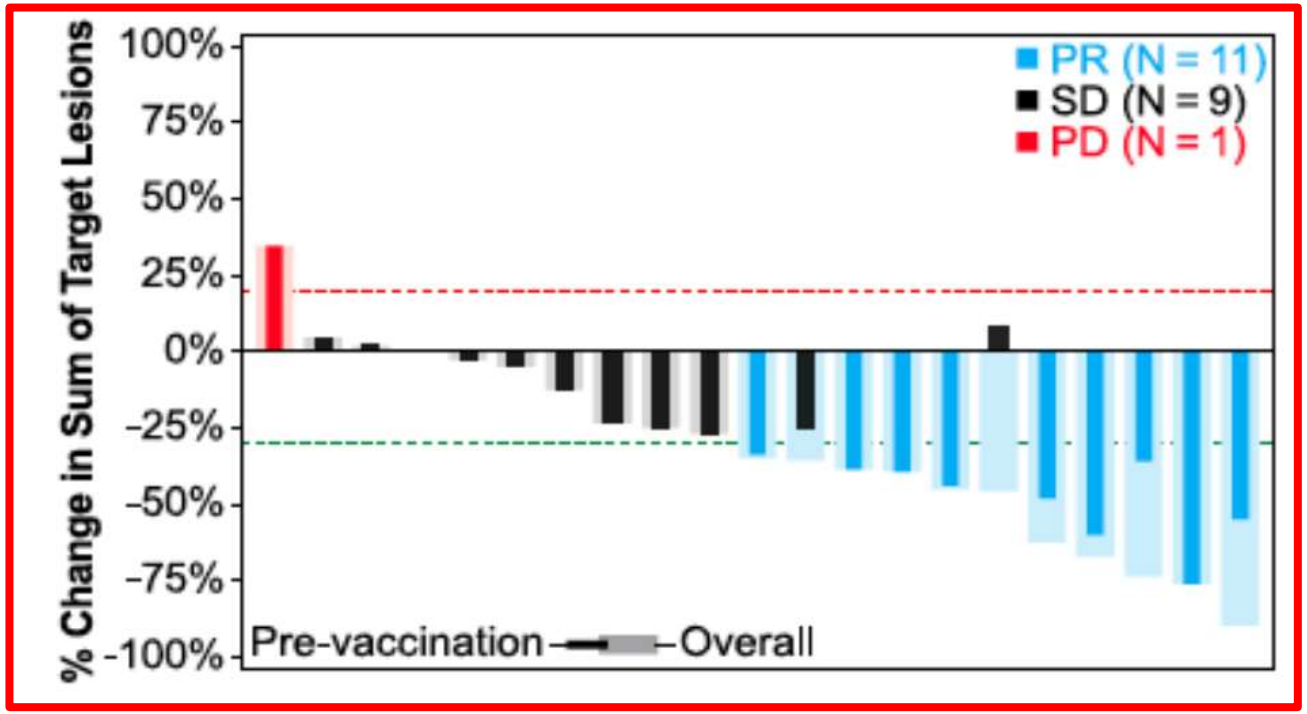
A personalized peptide vaccine of up to 20 unique peptides targeted toward high-quality neoepitopes identified using a bioinformatic algorithm



Awad Cancer Cell 2022

Personalized neoantigen vaccine NEO-PV-01 with chemotherapy and anti-PD1 as 1L treatment for non-squamous NSCLC





Awad Cancer Cell 2022

Cancer mRNA vaccines, BNT116

- BNT116 is an investigational **mRNA-LPX cancer immunotherapy utilizing mRNA-encoded tumor antigens** (CLDN6, KK-LC-1, MAGE-A3, MAGE-A4, MAGE-C1, PRAME) frequently expressed in NSCLC.
- RNA-LPX combines targeted antigen delivery with stimulation of a TLR-mediated type 1 interferon response.

Recruiting

Clinical Trial Evaluating the Safety, Tolerability and Preliminary Efficacy of BNT116 Alone and in Combinations in Patients With Advanced Non-small Cell Lung Cancer (LuCa-MERIT-1)

ClinicalTrials.gov ID NCT05142189
Sponsor BioNTech SE
Information provided by BioNTech SE (Responsible Party)
Last Update Posted 2025-11-12

Study Overview

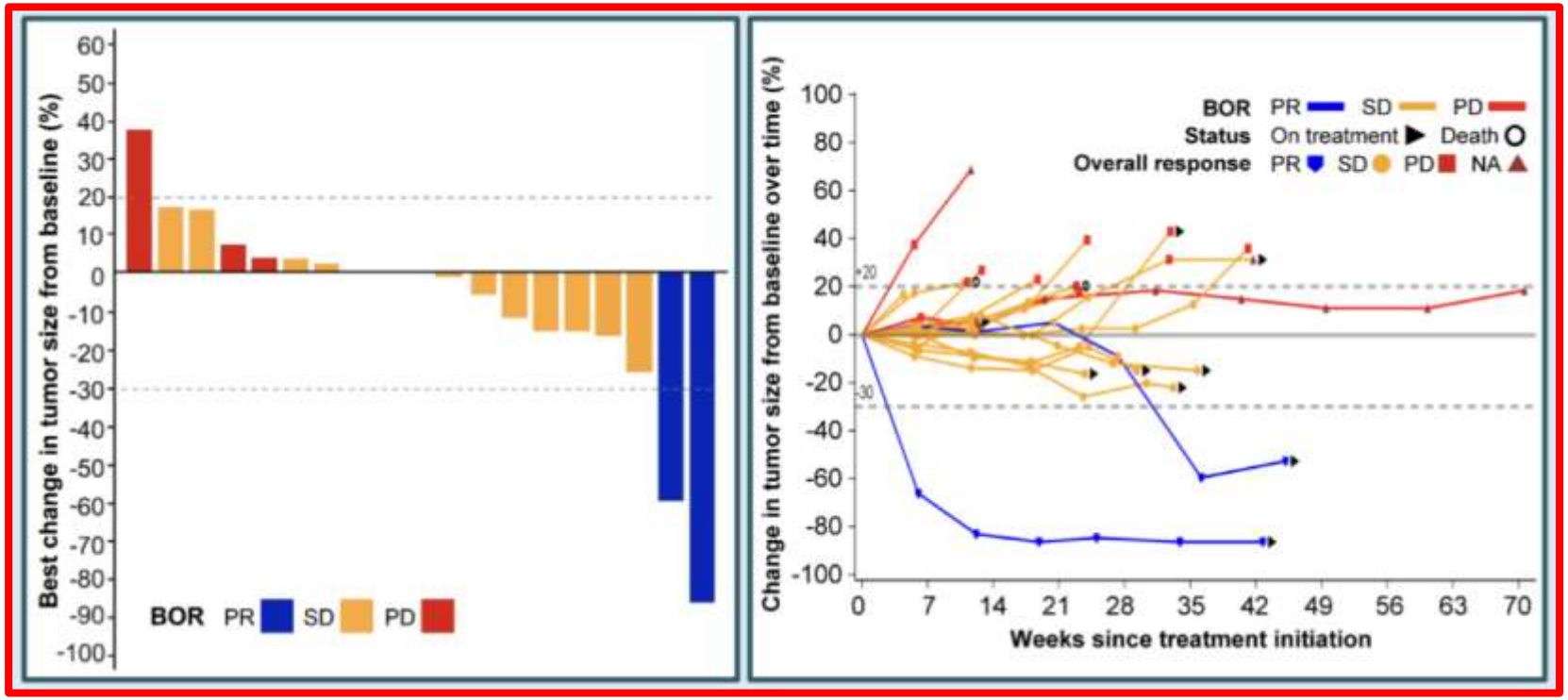
Brief Summary

This first-in-human (FIH) trial for BNT116 aims to establish the safety profile and a safe dose for BNT116 monotherapy as well as for BNT116 in combination with approved medicinal products and/or in combination with investigational medicinal products (IMPs) including, but not limited to, cemiplimab, docetaxel, carboplatin, paclitaxel, BNT316 (an anti-cytotoxic T-lymphocyte-associated protein 4 [CTLA-4] antibody), an anti-B7-H3 antibody conjugated to a topoisomerase I inhibitor, an anti-human epidermal growth factor receptor 3 (HER3) antibody conjugated to a topoisomerase I inhibitor or a bispecific antibody for programmed death ligand 1 (PD-L1) and vascular endothelial growth factor A (VEGF-A) in participants with non-small cell lung cancer (NSCLC).

The trial will comprise of several cohorts for dose confirmation in monotherapy as well as in combinations of BNT116 as mentioned above.

The trial will enroll participants with NSCLC in advanced or metastatic stage in Cohorts 1 to 4 and Cohorts 7 to 10, unresectable NSCLC Stage III in Cohorts 5 and 11, and resectable NSCLC of Stage II and III in Cohort 6.

Preliminary results from LuCa-MERIT-1, a Phase I trial evaluating BNT116, a fixed antigen mRNA vaccine, plus cemiplimab in advanced non-small cell lung cancer after progression on PD-1 inhibition



- 20 patients included, 2 PR, DCR 80%, mPFS 5.5 months, 12 months PFS rate 47%
- Flu-like symptoms

Atmaca ITC 2024

LuCa-MERIT-1 cohort 4: open label in frail NSCLC patients

Treatment Schedule

BNT116
7xq1w ("priming") then q3w ("maintenance")

D1 D8 D15 D1 D8 D15 D1 D1 D1 — Treatment until 24 months, confirmed PD, withdrawal of consent, or unacceptable toxicity

C1 C2 C3 C4 C5

Priming | Maintenance

Cemiplimab

Sampling for mandatory biomarker assays and optional PBMC collections for immunomonitoring

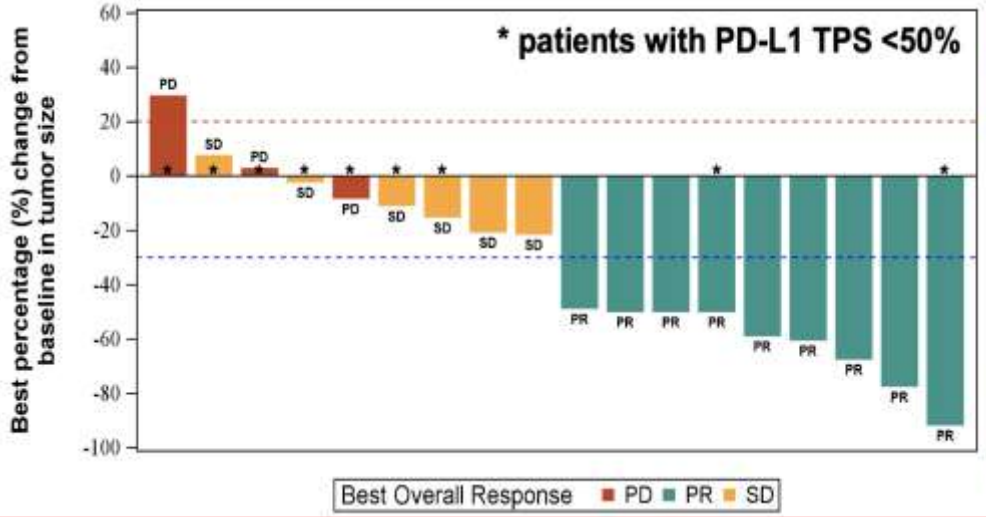
Patients

Key inclusion criteria
- Unresectable Stage III or metastatic Stage IV NSCLC (any histologic subtype)
- Patients who are not candidates for chemotherapy as first-line treatment for advanced or metastatic NSCLC
- Positive PD-L1 expression of TPS ≥1% in tumor cells
- ECOG PS 0 to 2

Key exclusion criteria
- Patients having received a prior systemic therapy as first-line treatment for advanced or metastatic NSCLC

Endpoints

- **Primary**: Safety (DLTs, TEAEs) and tolerability
- **Secondary**: Efficacy per RECIST 1.1 (investigator assessed): ORR, PFS, DCR, DoR, DoDC, OS
- **Exploratory**: Evaluate predictive and pharmacodynamic biomarkers



RECIST 1.1, investigator	LuCa-MERIT-1 frail NSCLC patients (N=20)
Best overall response, n (%)	
PR	9 (45.0%)
SD	6 (30.0%)
PD	3 (15.0%)
Missing	2 (10.0%)
ORR (%)	45.0%
DCR (%)	75.0%

Data cut-off date: March 1, 2025

- Median PFS 9.9 months
- BNT116-induced responses against each antigen were assessed by *ex vivo* ELISpot.
- A high immunogenicity rate was observed with at least 5/7 (71%) patients having a *de novo* response to at least one TAA.
- All frail patients (19/19) were able to mount a robust type 1 interferon cytokine response.

Dziadzuisko AACR 2025

LuCa-MERIT-1 advanced NSCLC patients with previous cCRT

Patients

Key inclusion

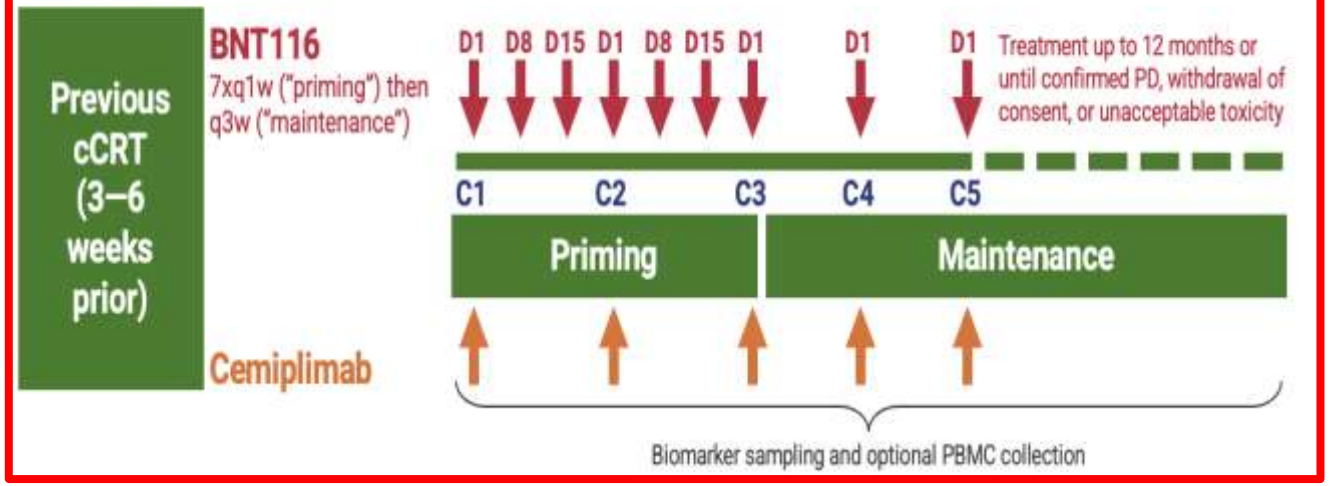
- Unresectable Stage III NSCLC
- cCRT shortly before entering the trial
- Able to tolerate anti-PD-1
- ECOG PS 0 to 2

Key exclusion

- Prior systemic therapy or radiation therapy except for CRT
- Progressive disease after CRT

- This cohort evaluates BNT116 plus cemiplimab as consolidation treatment in patients with advanced NSCLC after prior SOC cCRT.

Treatment schedule



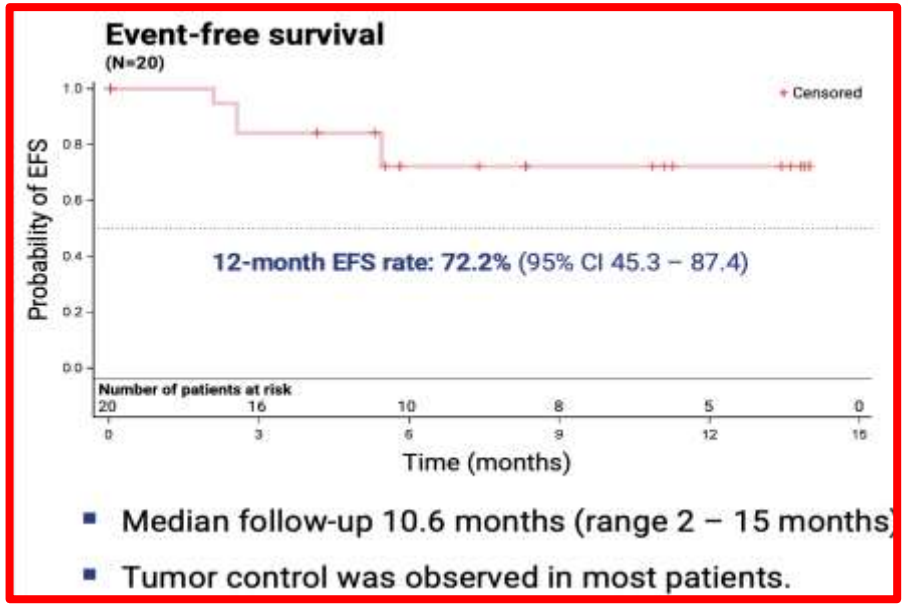
LuCa-MERIT-1 advanced NSCLC patients with previous cCRT

Patient characteristics at baseline	BNT116 plus cemiplimab N = 20
Age (years)	
Median	67.5
Range	42 – 82
PD-L1 expression of TPS in tumor cells, n (%)	
<1%	5 (25)
1–49%	8 (40)
≥50%	7 (35)
ECOG PS, n (%)	
0	6 (30)
1	14 (70)
NSCLC histopathological subtype, n (%)	
Adenocarcinoma	3 (15)
Squamous-cell carcinoma	17 (85)
Tumor stage, n (%)	
IIIA	5 (25)
IIIB	12 (60)
IIIC	2 (10)
Other	1 (5)

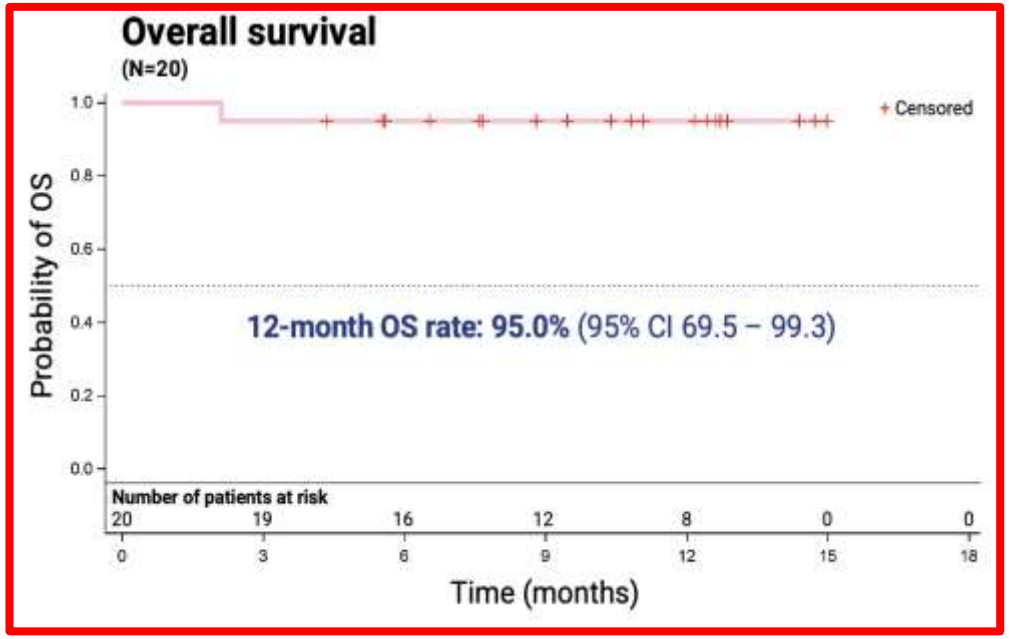
LuCa-MERIT-1 advanced NSCLC patients with previous cCRT

Patients with at least one, n (%)	BNT116 plus cemiplimab N = 20
TEAE (all grades)	20 (100)
Related to BNT116*	20 (100)
Related to cemiplimab	15 (75)
TEAE Grade ≥ 3	12 (60)
Related to BNT116	6 (30)
Cytokine release syndrome	2 (10)
Infusion related reaction	1 (5)
Hypoxia	1 (5)
Pneumonitis	2 (10)
Hypertension	1 (5)
Related to cemiplimab	4 (20)
TEAE with fatal outcome	0
Serious TEAE related to BNT116	4 (20)
Cytokine release syndrome**	2 (10)
Pneumonitis***	2 (10)
Dermatitis related to treatment	
Grade 1	1 (5)
Grade ≥ 2	0
Pneumonitis related to treatment	
Grade 1/2	3 (15)
Grade 3	2 (10)

* 70% Grade 1 and 2; ** both Grade 3, recovered within 24 h; *** both Grade 3, serious for 7–8 d, recovered/recovering (downgrading of severity to Grade 1) 26–28 d.

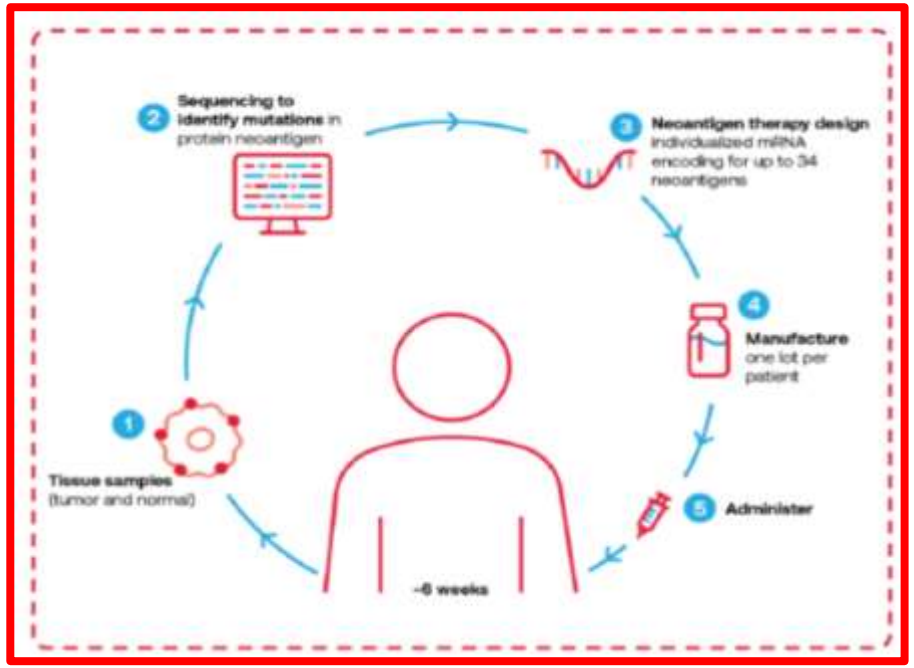


- Median follow-up 10.6 months (range 2 – 15 months)
- Tumor control was observed in most patients.

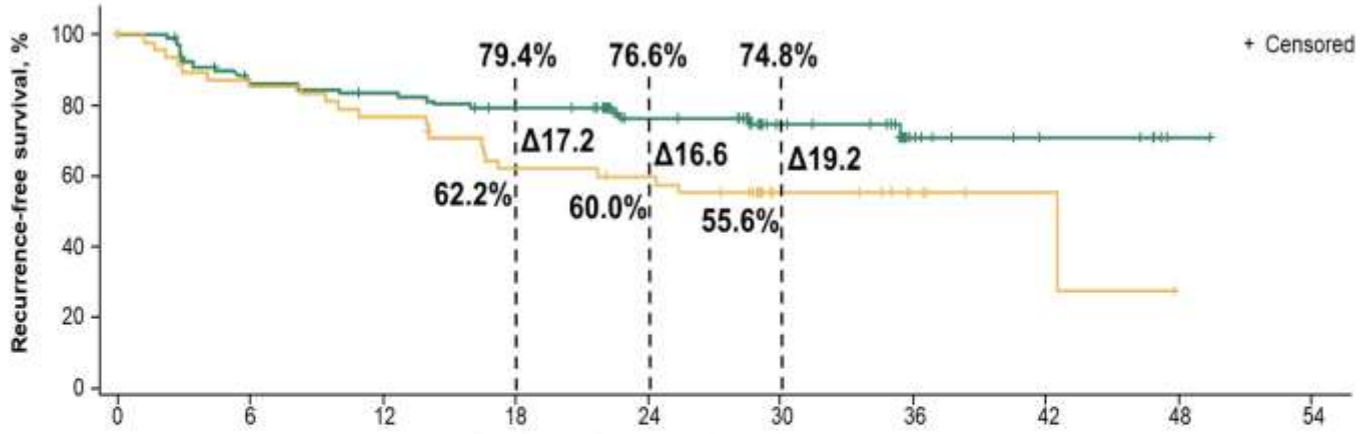


mRNA-4157 (V940) individualized neoantigen therapy, melanoma

V940 (mRNA-4157) is a novel individualized neoantigen therapy that encodes up to 34 personalized neoantigens



Sustained improvement of RFS primary efficacy endpoint



Patients at risk										
mRNA-4157 (V940) + pembrolizumab	107	87	83	77	52	29	12	6	1	0
Pembrolizumab	50	41	37	29	27	10	5	2	0	0

	Median (95% CI), months	Events, % (n/N)	Hazard ratio (95% CI)[a]
mRNA-4157 (V940) + pembrolizumab	NE	23.4 (25/107)	0.510 (0.288–0.906) *P* = 0.019[b]
pembrolizumab	42.51 (16.59–NE)	44.0 (22/50)	

NCI Drug Dictionary. mRNA-4157, Khattak AACR 2023; Weber Lancet 2024

T-cell responses to individualized neoantigen therapy mRNA-4157 (V940) alone or in combination with pembrolizumab in the phase 1 KEYNOTE-603 study

KEYNOTE-603 Study

Up to 34 neo-antigens

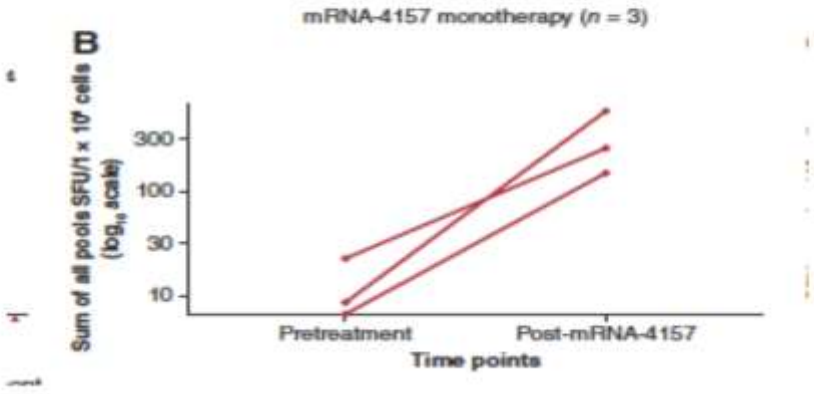
Adjuvant treatment in 4 NSCLC patients

Short follow up no recurrence

Beneficial safety profile, also with PD-1

- pyrexia
- fluw like syndrome
- infection site reaction

Gainor Cancer Discov 2024



Study	Phase	N	Population	Intervention	PEP	NCT
INTerpath-002	III	868	Resected II-IIIB (N2) NSCLC No neoadjuvant Prior adjuvant chemo No EGFR	V490 q3w x9 cycles + pembro 400mg q6w x7 cycles vs placebo+ pembro 400mg q6w x7 cycles	DFS	NCT06077760
INTerpath-009	III	680	Resected II-IIIB (N2) NSCLC No pCR after neoadjuvant pembrolizumab + chemo	V490 q3w x9 cycles + pembro 400mg q6w x7 cycles vs placebo+ pembro 400mg q6w x7 cycles	DFS	NCT06623422

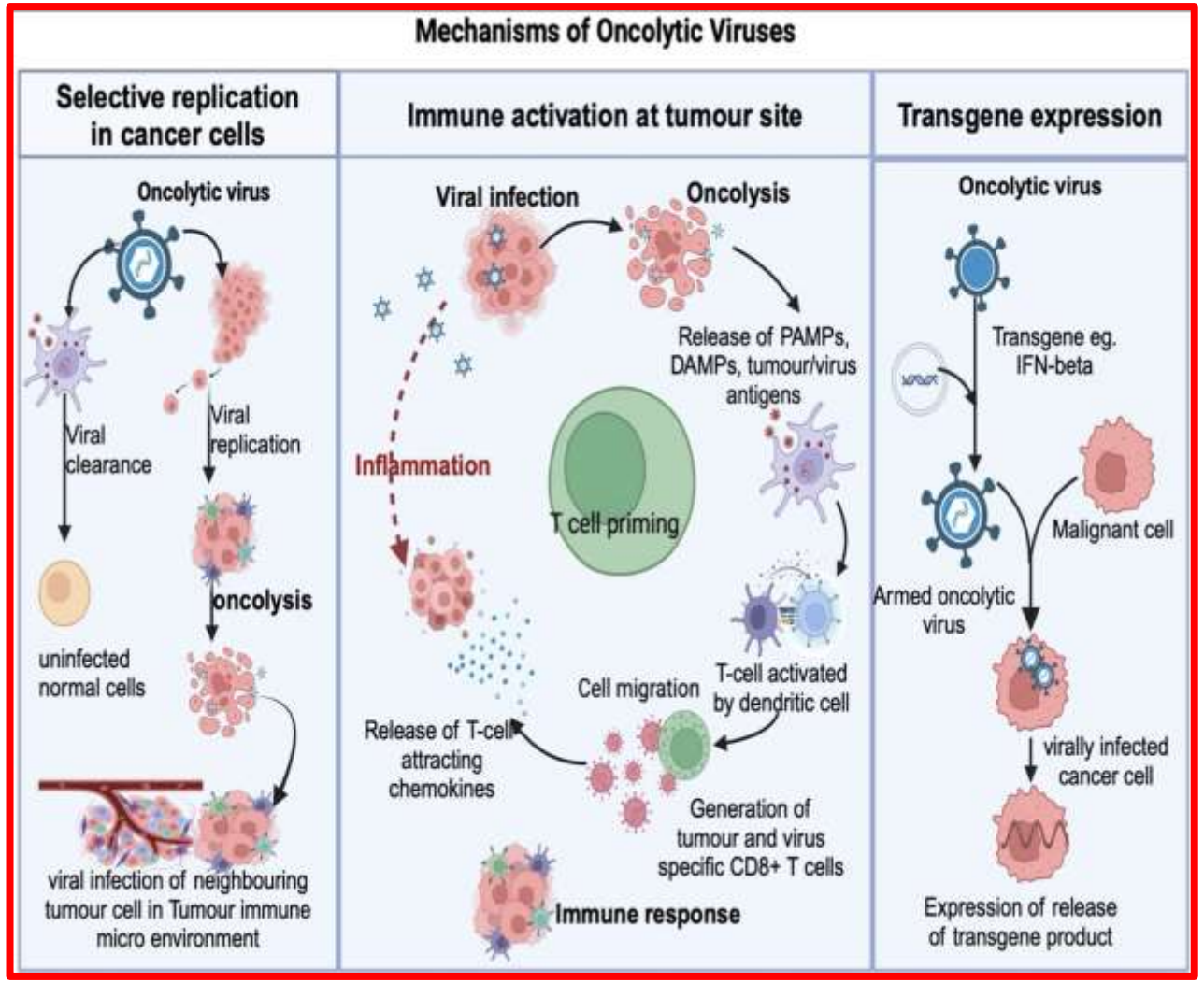
Oncolytic virus

Oncolytic viruses, potential benefits of selective replication in tumour cells, induction of immunogenic cell death and promotion of antitumour immunity

Oncolytic viruses are modified or naturally occurring viruses that preferentially infect and replicate inside cancer cells, eventually destroying them

As the viruses destroy cancer cells, they also trigger an immune response that targets both the infected cells and other cancer cells, even in distant parts of the body

They can be combined with other treatments



Steele Cancer Treatment and Research Communications 2025

Oncolytic virus

EMA approved in 2015 Talimogene laherparepvec (T-VEC) an intralesionally delivered oncolytic immunotherapy comprised of a genetically engineered attenuated herpes simplex virus type 1 of the JS-1 strain and was approved for the treatment of patients with recurrent melanoma after initial surgery

23/10/15

A viral immunotherapy for cancer has become the first to be given the green light by European regulators.

The treatment, called Talimogene laherparepvec, or T-VEC for short, has been recommended for approval by the European Medicines Agency for use in adults with advanced melanoma.

Researchers from The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust **led the UK arm of a major phase III trial showing that T-VEC was effective in patients**.

If fully approved, T-VEC would be the first in a whole new type of cancer treatment called **oncolytic immunotherapy** – which targets cancer cells with viruses and directs the immune system against them.

T-VEC is a modified form of the herpes simplex virus which multiplies inside cancer cells and bursts them from within. It has been genetically engineered to produce a molecule called GM-CSF, which stimulates the immune system to attack and destroy the tumour.

Clinical Trial > J Clin Oncol. 2015 Sep 1;33(25):2780-8. doi: 10.1200/JCO.2014.58.3377. Epub 2015 May 26.

Talimogene Laherparepvec Improves Durable Response Rate in Patients With Advanced Melanoma

Robert H I Andtbacka [1], Howard L Kaufman [2], Frances Collichio [1], Thomas Amatruda [1],

Results: Among 436 patients randomly assigned, DRR was significantly higher with T-VEC (16.3%; 95% CI, 12.1% to 20.5%) than GM-CSF (2.1%; 95% CI, 0% to 4.5%]; odds ratio, 8.9; P < .001). Overall response rate was also higher in the T-VEC arm (26.4%; 95% CI, 21.4% to 31.5% v 5.7%; 95% CI, 1.9% to 9.5%). Median OS was 23.3 months (95% CI, 19.5 to 29.6 months) with T-VEC and 18.9 months (95% CI, 16.0 to 23.7 months) with GM-CSF (hazard ratio, 0.79; 95% CI, 0.62 to 1.00; P = .051). T-VEC efficacy was most pronounced in patients with stage IIIB, IIIC, or IVM1a disease and in patients with treatment-naive disease. The most common adverse events (AEs) with T-VEC were fatigue, chills, and pyrexia. The only grade 3 or 4 AE occurring in ≥ 2% of T-VEC-treated patients was cellulitis (2.1%). No fatal treatment-related AEs occurred.

Oncolytic virus, challenges and limitations

A better understanding of the underlying biology and pharmacology of OVs is needed

Challenges such as limited tumor penetration and spread, the host's immune system clearing the virus too quickly, and the need for direct injection into tumors

- **Delivery and spread:** A major hurdle is getting the virus to the tumor. Many current methods require direct,intratumoral injection to ensure the virus isn't eliminated before it reaches the target
- **Host immune response:** The body's natural immune response can neutralize the virus before it has a chance to infect and destroy tumor cells, particularly with systemic (intravenous) administration
- **Tumor barriers:** The physical and biological barriers within the tumor microenvironment can limit how far the virus can spread
- **Potential side effects:** While generally well-tolerated, side effects like fever, fatigue, chills, and pain at the injection site can occur

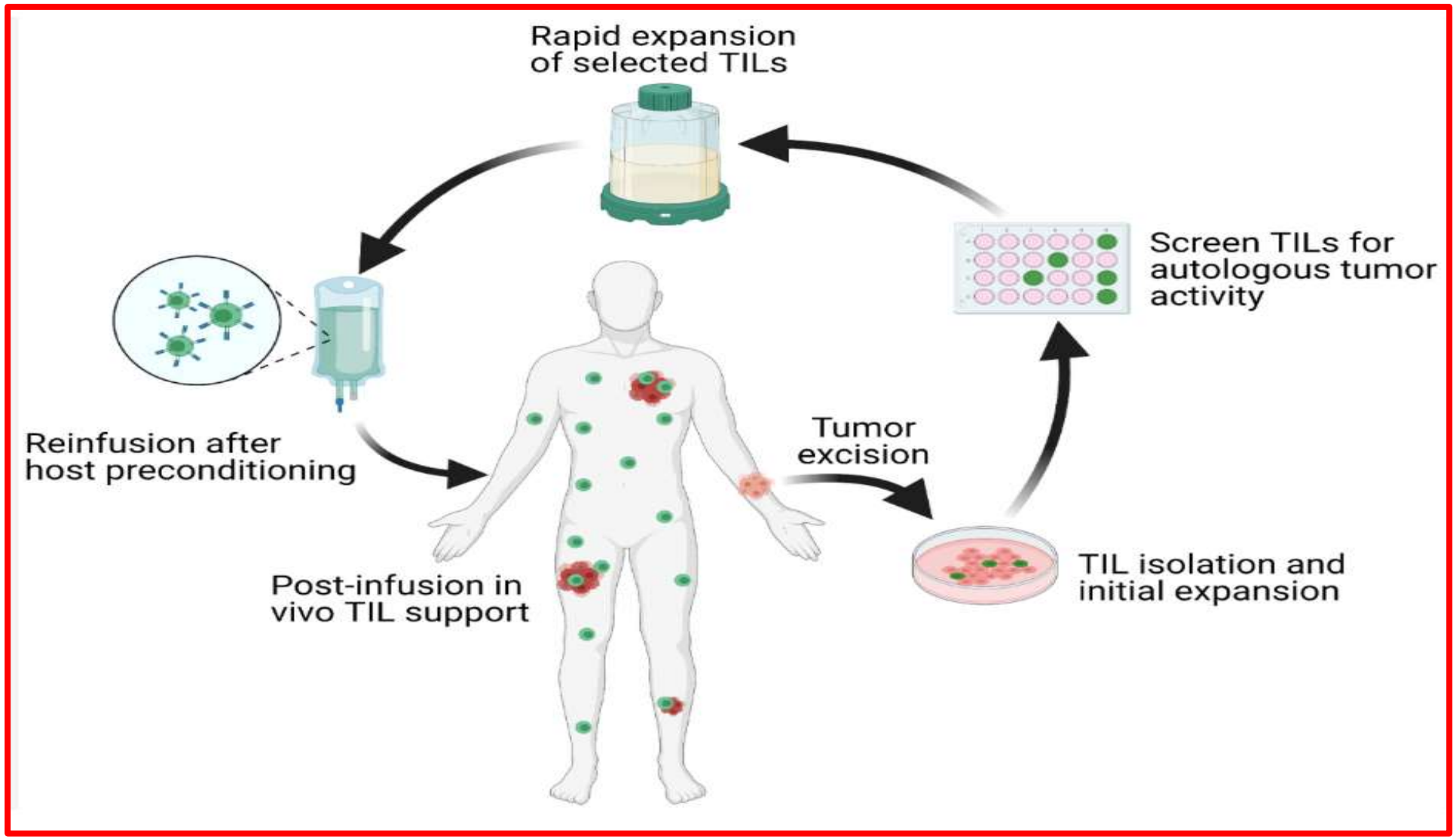
Therapy gone viral: exploring the use of oncolytic virus in NSCLC

Steele Cancer Treatment and Research Communications 2025

Table 1
Table of clinical trials using OVs in NSCLC treatment.

Clinical Trial	Oncolytic virus	Phase	Associated reports of trial	Registration number
Adenovirus				
ADV/HSV-tk SBRT and Oncolytic Virus Therapy Before Pembrolizumab for Metastatic TNBC and NSCLC (STOMP)	ADV/HSV-tk adenovirus/herpex simplex-thymidine kinase/ ganciclovir	II	A Phase 2 study of In Situ Oncolytic Virus Therapy and Stereotactic Body Radiation Therapy Followed by Pembrolizumab in Metastatic Non-small Cell Lung Cancer	NCT03004183
MEM288 Study of MEM-288 Oncolytic Virus in Solid Tumours	MEM-288 a conditionally replicative oncolytic adenovirus. Encodes immune agonists: human IFNβ and a membrane-stable form of CD40L	I	Combination IFNβ and membrane stable CD40L maximise tumour dendritic cell activation and lymph node trafficking to elicit systemic T-cell immunity	NCT05076760
CAdVEC Binary Oncolytic Adenovirus in Combination With HER2-Specific Autologous CAR VST, Advanced HER2 Positive Solid Tumours (VISTA)	CAdVEC A genetically modified oncolytic viral strain of human adenovirus (Ad) with potential immunostimulating and antineoplastic activities	I	Still recruiting Ultralow-dose binary oncolytic/helper-dependent adenovirus promotes antitumor activity in preclinical and clinical studies	NCT03740256
L-IFN Safety and Efficacy of Recombinant Oncolytic Adenovirus L-IFN Injection in Relapsed/Refractory Solid Tumours	Recombinant L-IFN Recombinant Oncolytic Adenovirus	I	Study ongoing Double-edged effects of interferons on the regulation of cancer-immunity cycle	NCT05180851
Ad/MGI-MAGEA3 **MAGE-A3** protein is expressed in approximately 35 % of patients with resectable NSCLC	Ad/MGI-MAGEA3 rhabdovirus Maraba MAGE-A3 mouse model	I	Phase 1b open-label dose escalation trial of Ad/MG1-MAGEA3 and Pembrolizumab in patients with Metastatic Melanoma	NCT02879760
Reovirus				
REOLYSIN in combination with Paclitaxel and Carboplatin for NSCLC With KRAS or EGFR Activation Combination with Paclitaxel and Carboplatin for NSCLC With KRAS or EGFR Activation	Pelareorep Unmodified human reovirus Wild type reovirus + Paclitaxel	II II	Oncolytic Reovirus in Combination With Chemotherapy in Metastatic or Recurrent Non–Small Cell Lung Cancer Patients With KRAS-Activated Tumours To investigate whether intravenous administration of a wild type reovirus (REOLYSIN®) in combination with paclitaxel	NCT00861627 NCT00861627
Measles Virus				
RT-01 Measles Virus (Edmonston Strain) in patients with metastatic NSCLC	RT-01\ Measles in Combination With Atezolizumab	I	Phase 1 Dose Escalation Trial of Intra-Tumoral Injection of Sodium Iodide Simporter (NIS) Measles Virus (Edmonston Strain) in combination with Atezolizumab in patients with metastatic NSCLC	NCT02919449
Alphavirus				
VRT106 The therapeutic candidate is recombinant oncolytic virus M1 of alpha virus (M1-c6v1).	Alphavirus M1-c6v1	I	M1-c6v1 is under development for the treatment of advanced or metastatic solid tumour, hepatocellular carcinoma, liver cancer, cervical cancer, triple-negative breast cancer, colorectal cancer, prostate cancer, melanoma and malignant glioma, administered through intravenous drip and intratumor route.	NCT06826313 NCT06758544
Herpes Simplex Virus				
HSV1716 (Seprehvir) is a replication restricted oncolytic herpes simplex virus with anti-tumour effects in multiple cell lines including Malignant Pleural Mesothelioma (MPM). Oncolytic herpesvirus therapy for mesothelioma -	Herpes Simplex Intrapleural HSV1716 was well-tolerated and demonstrated an anti-tumour immune response in MPM patients.	I / IIa	Intrapleural HSV1716 was well-tolerated and demonstrated an anti-tumour immune response in MPM patients. These results provide a rationale for further studies with this agent in MPM and in combination with other therapies	NCT00931931
YD06-1 The Application of Novel Oncolytic Virus in Late-Stage Solid Tumours The purpose of this study is to evaluate the efficacy and safety of novel oncolytic virus in late-stage solid tumours.	Herpes Simplex with nucleic acid sequence of the gRNA targeting the ICP34.5 gene is shown in SEQ ID NO: 3, and the nucleic acid sequence of the gRNA targeting the ICP47 gene	I / II	Active recruiting The Application of Novel Oncolytic Virus in Late-Stage Solid Tumours Cancer patients receive intratumoral treatment with a novel oncolytic virus YD06-1	NCT06080984
R130 Clinical trial to evaluate the safety, tolerability, and efficacy of the recombinant HSV-I in lung cancer	Herpes Simplex Anti-CD3 scFvCD86/PD/HSV2-US11 insertion	I	Oncolytic virotherapy against lung cancer: key receptors and signalling pathways of viral entry	NCT05886075 NCT05961111 NCT05860374 NCT05801783
Vaccinia Virus				
CF33-hNIS CF33-hNIS monotherapy may be an effective and has the potential to act as both a gene therapy delivery vehicle and an oncolytic (cancer-killing) agent	Vaccinia. Imugene as a combination of genomic sequences from multiple vaccinia virus strains, generating a new, safer, and more potent virus safe treatment	I	Investigators Launch Study to Review Novel Cancer Vaccine in Patients with Advanced Solid Tumours A Study of CF33-hNIS (VAXINIA), an Oncolytic Virus, as Monotherapy or in Combination With Pembrolizumab in Adults With Metastatic or Advanced Solid Tumours	NCT05346494
V937 purpose of this trial is to assess the ability of CVA21, either alone (Part A) or in combination with pembrolizumab (Part B), to reach and to replicate in existing tumours (while sparing normal cells) and to establish a safe multi-dose schedule of the virus for the treatment of solid tumours where enhanced expression of ICAM-1 and/ or DAF receptor occurs	VLA-009A and VLA-009B are open-label, multi-centre, ascending dose escalation (3 + 3 design) dose-finding and signal-seeking studies efficacy of intratumoral administration of CF33-hNIS-anti-PD-L1 (CHECKvacc) against mTNBC	I / II	Phase 2 Study of V937 Plus Pembrolizumab	NCT02043665
BT-001 BT-001 is an oncolytic vaccinia virus with enhanced replication selectivity in tumour cells and recombinantly armed to express GM-CSF and an anti-CTLA-4 mAb	Pembrolizumab KEYTRUDA®].. humanized monoclonal antibody Chimeric 4-E03/GM-CSF	I/II	Recruiting 594BT-001, an oncolytic vaccinia virus armed with a Treg-depleting human recombinant anti-CTLA4 antibody and GM-CSF to target the tumour microenvironment 1024P Initial clinical results of BT-001, an oncolytic virus expressing an anti-CTLA4 mAb, administered as single agent and in combination with pembrolizumab in patients with advanced solid tumours	

Adoptive cellular therapy: Tumor-inflitrating lymphocyte (TILs)
Tumour extraction required



Quin Cells 2021

Adoptive cellular therapy: TILs

Lifileucel, autologous TIL, was successfully manufactured using tumor tissue from different anatomic sites, predominantly lung

Cancer Discovery 2024

Lifileucel, an Autologous Tumor-Infiltrating Lymphocyte Monotherapy, in Patients with Advanced Non-Small Cell Lung Cancer Resistant to Immune Checkpoint Inhibitors

Adam J. Schoenfeld[1], Sylvia M. Lee[2], Bernard Doger de Spéville[3], Scott N. Gettinger[4], Simon Häfliger[5], Ammar Sukari[6], Sophie Papa[7,8], Juan F. Rodriguez-Moreno[9], Friedrich Graf Finckenstein[10], Rana Fiaz[10], Melissa Catlett[10], Guang Chen[10], Rongsu Qi[10], Emma L. Masteller[10], Viktoria Gontcharova[10], and Kai He[11]

Table 3. Efficacy outcomes by investigator assessment.

Response (RECIST v1.1)	Full analysis set ($N = 28$)
ORR, *n* (%) (95% CI)	6/28 (21.4) (8.3–41.0)
BOR, *n* (%)	
CR[a]	1/28 (3.6)
PR	5/28 (17.9)
SD	12/28 (42.9)
PD	6/28 (21.4)
Non-evaluable	4/28 (14.3)
DOR, months (range)	1.1+ to 26.2+
DOR for patient with CR, months	26.2+
DOR for patients with PR, months	8.7+, 4.2, 2.6, 2.4, 1.1+

	Full analysis set ($N = 28$)		
TEAEs (≥20%)	Any grade *n* (%)	Grade 3/4 *n* (%)	Grade 5 *n* (%)
Number of patients reporting ≥1 TEAE	28 (100.0)	27 (96.4)	2 (7.1)[b]
Chills	19 (67.9)	1 (3.6)	0
Hypotension	18 (64.3)	7 (25)	0
Pyrexia	16 (57.1)	1 (3.6)	0
Hypoxia	15 (53.6)	5 (17.9)	0
Alopecia	10 (35.7)	0	0
Diarrhea	10 (35.7)	3 (10.7)	0
Peripheral edema	10 (35.7)	0	0
Decreased appetite	9 (32.1)	3 (10.7)	0
Dyspnea	9 (32.1)	3 (10.7)	0
Fatigue	9 (32.1)	4 (14.3)	0
Febrile neutropenia	8 (28.6)	8 (28.6)	0
Nausea	8 (28.6)	1 (3.6)	0
Hypertension	7 (25.0)	6 (21.4)	0
Hypokalemia	7 (25.0)	2 (7.1)	0
Sinus tachycardia	7 (25.0)	0	0
Vomiting	7 (25.0)	0	0
Constipation	6 (21.4)	0	0
Capillary leak syndrome	6 (21.4)	1 (3.6)	0
Headache	6 (21.4)	0	0
Pleural effusion	6 (21.4)	1 (3.6)	0
Weight decreased	6 (21.4)	0	0

Hematologic laboratory abnormalities	Full analysis set ($N = 28$) Grade 3/4
Low leukocytes	28 (100)
Low lymphocytes	28 (100)
Low neutrophils	28 (100)
Low platelets	27 (96.4)
Low hemoglobin	19 (67.9)

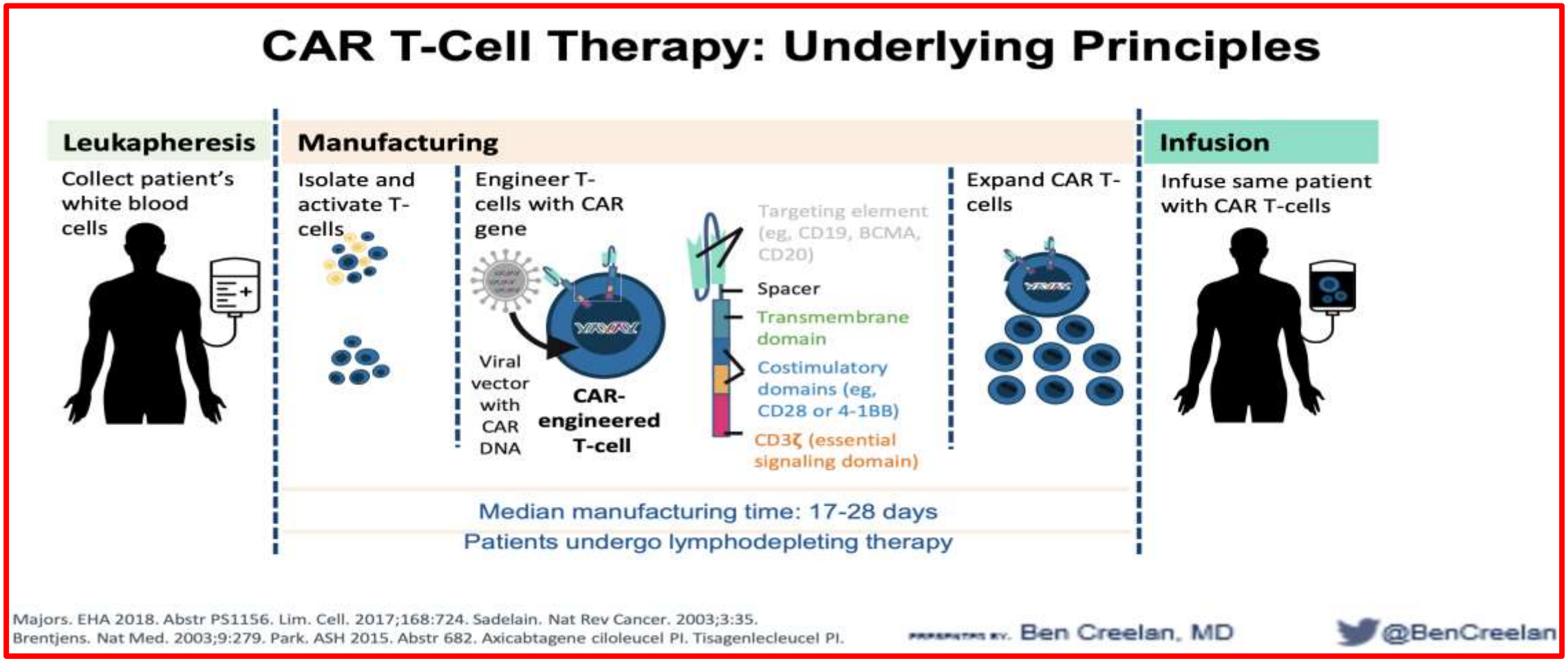
Overview of Ongoing TIL trials w/ NSCLC Patients

Summary of Known Trials

Therapy	Sponsor	NeoAg-enrich?	Genetic edit?	Sample Size	Prior aPD1?	CyFlu, IL2?	NCT ID
CD40L TIL	Moffitt	No	No	20	No	Yes, Yes	05681780
ATX-001	Achilles	Yes	No	50	Yes	Yes, Yes*	04032847
NeoTIL	CHUV	Yes	No	42	Yes	Yes, Yes	04643574
CheckCell-2	Intima	Yes	Yes, CISH	70	Yes	Yes, Yes	05566223
NextGen-TIL	VHIO	Yes	No	10	Yes	Yes, Yes	05141474
Lifeleucil	Iovance	No	No	95	Yes	Yes, Yes	04614103
IOV-4001	Iovance	No	Yes, PD1	53	Yes	Yes, Yes	05361174
ITIL-306	Instil Bio	No	Yes, FR	51	Yes	Yes, No	05397093
Lifeleucil	Iovance	No	No	178	No	Yes, Yes	03645928
C-TIL051	CBMG	No	No	20	No	Yes, Yes	05676749
OBX-115	Obsidian	No	Yes	52	Yes	Yes, No	06060613

Adoptive cellular therapy: CAR-T
Targets cell surface Ag only

CAR T cells are genetically modified T lymphocytes that express a chimeric receptor specific for a tumor antigen

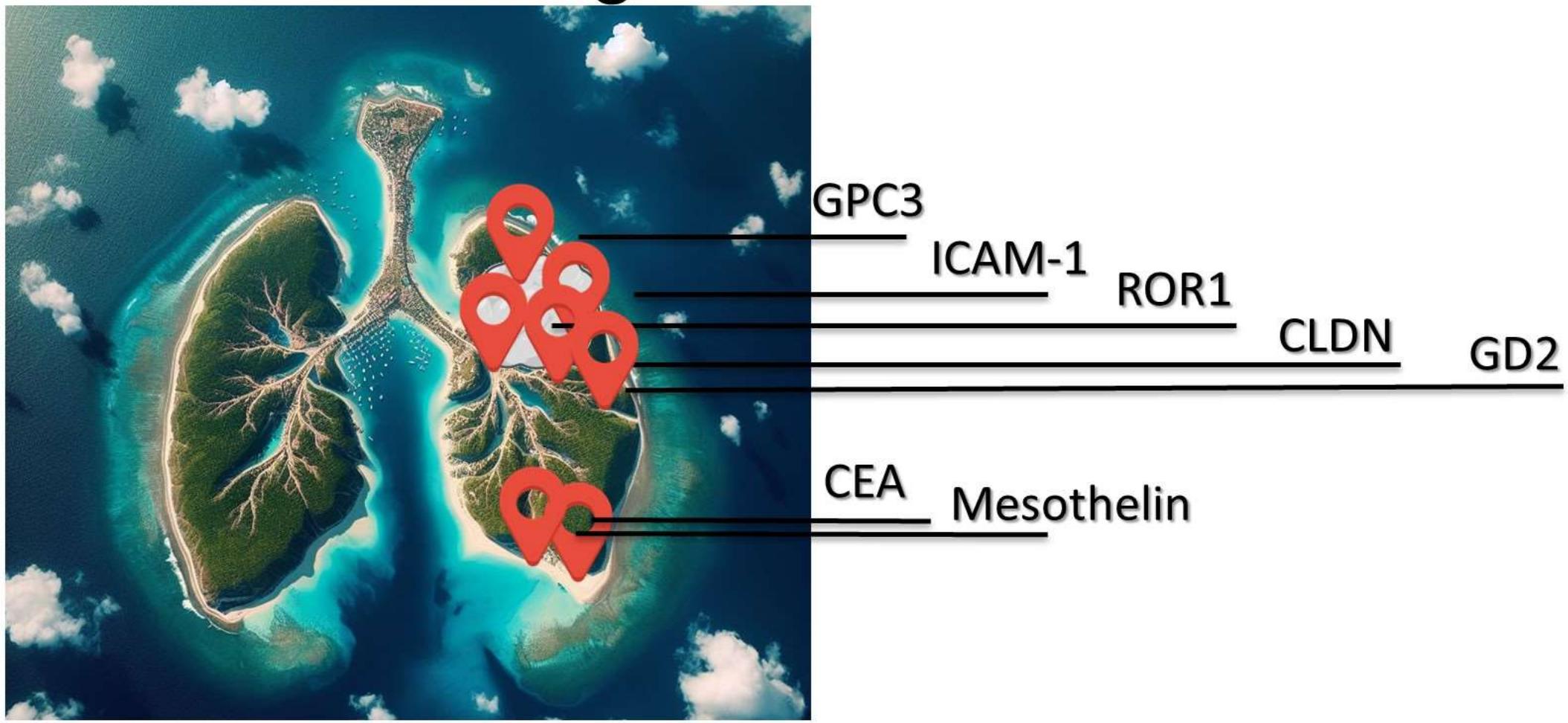


Adoptive cellular therapy: CAR-T

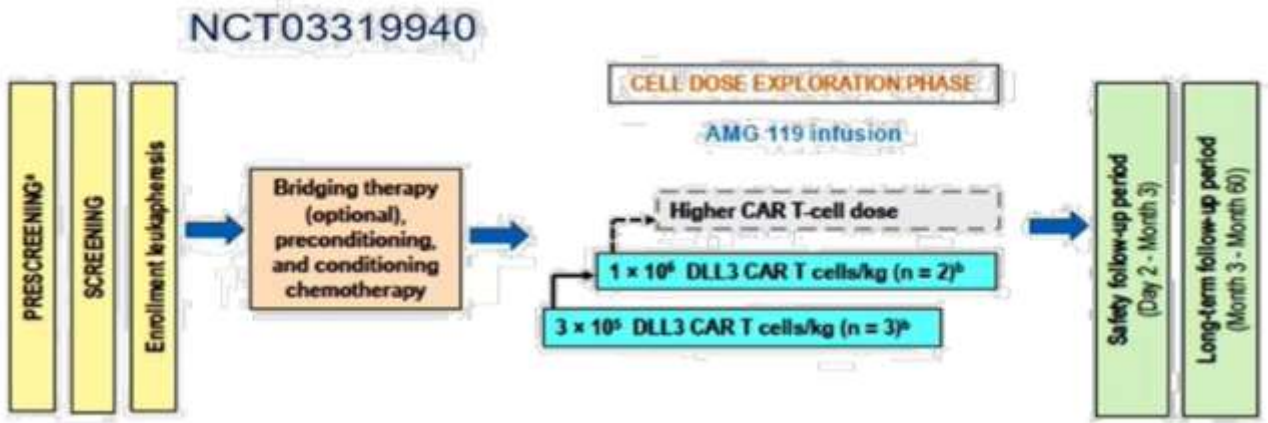
Target	Treatment	Pt population	Outcomes
Mesothelin	Gavo-cel	Solid tumours	ORR: 20%[1]
CLND6	CLDN6 CAR T + CARVac	Solid tumours	ORR: 41.7%[2]
GPC3	GPC3 CAR T 15.GPC3 CAR	Solid tumours	ORR: 0%[3] ORR: 33%[3]

1. Hassan Nat Med 2023, Haanen ESMO 2024, 3. Steffin Nature 2025

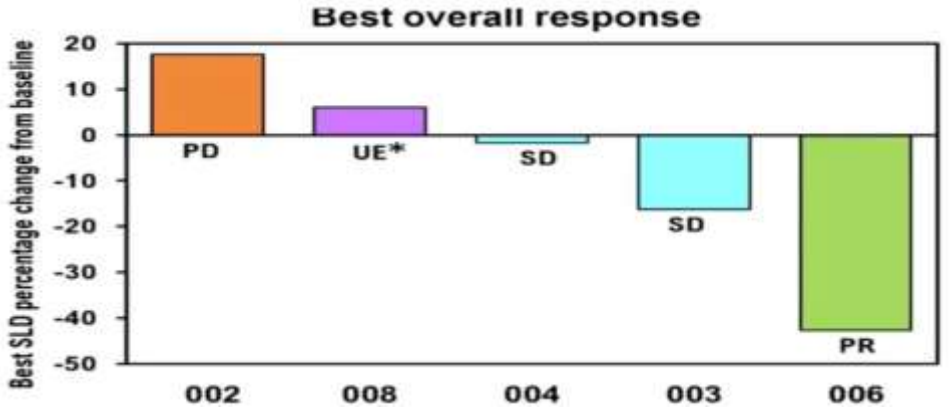
Mapping Lung Cancer: CAR & BiTE Targets



AMG119 a CAR-T for DLL3 in SCLC: Ph1 trial



Byers SITC 2022



- AMG119: *n* = 5 treated R/R ED-SCLC
- No DLTs or G4 TEAEs
- Benefit correlated w/ DLL3 expression
- CAR persistence >86 days post-infusion

TABLE 2 Clinical study of CAR-T-based immunotherapy in SCLC.

Target	Drug	Study population	Clinical trial
DLL3	DLL3 CAR-T (AMG119)	ES-SCLC	Phase I NCT03392064[39]
DLL3	DLL3 CAR-T (LB2102)	ES-SCLC, large cell neuroendocrine lung carcinoma	Phase I NCT05680922
DLL3	DLL3 CAR-T (SNC-115 injection)	ES-SCLC, large cell neuroendocrine lung carcinoma	Phase I NCT06384482
DLL3	α-PD-L1/4-1BB DLL3 CAR-T (BHP01)	ES-SCLC	Phase I NCT06348797
GD2	iC9 GD2 CAR IL-15 T cells	SCLC, NSCLC	Phase I NCT05620342

Adoptive cellular therapy: CAR-T Challenges

CAR targeting tumor cell PD-L1

Terminated

Serious adverse events

CAR-T Cell Immunotherapy for Advanced Lung Cancer

ClinicalTrials.gov ID NCT03330834

Sponsor Sun Yat-sen University

Information provided by Li Zhang, MD, Sun Yat-sen University (Responsible Party)

Last Update Posted 2020-07-13

CAR T progress in solid tumors is challenging due to target availability, antigen heterogeneity, and the tumor microenvironment

16th CONGRESS Lung ON CANCER

BARCELONA 27 / 28 NOVEMBER 2025

THANK YOU!!!

GECP lung cancer research