# LUNG CANCER UPDATES

## AACR HIGHLIGHTS

**29 MARZO - 3 ABRIL 2019**


Iniciativa científica de:

GECP

Grupo Español de Cáncer de Pulmón

Spanish Lung Cancer Group

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ATLANTA

# Other Thoracic Malignancies and NSCLC Driver mutations

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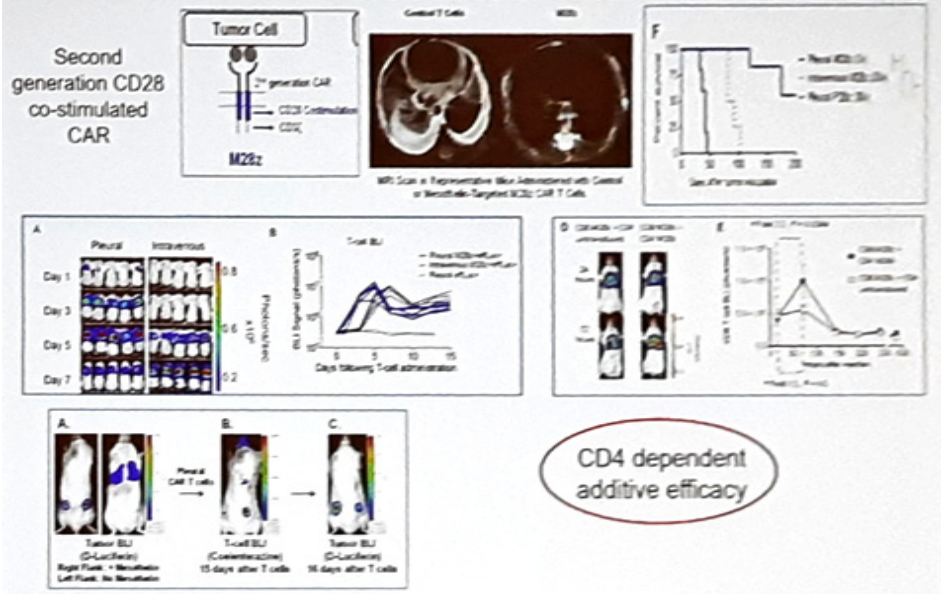
*Mesothelin-targeted CAR T-cell therapy*

## Intrapleural administration potentiates CAR T-cell efficacy

Second generation CD28 co-stimulated CAR




Adusumilli PS, Sadelain M. *Sci Transl Med* 2014

*Mesothelin-targeted CAR T-cell therapy*

## Intrapleural CAR T cells are well tolerated

On-target, off-tumor toxicity monitoring

| Monitored by | Method |
|---|---|
| Clinical | Pleuritis<br>Pericarditis<br>Peritonitis |
| Laboratory | Serum Troponin level |
| Cardiac | EKG, Echocardiogram |
| Imaging | CXR, CT, PET |
| Pathology | Biopsy |

| Adverse event | Grade | # of patients |
|---|---|---|
| Fever and chills | 1 | 6 |
| CRS (Cytokine release syndrome) | 1 | 3 |
| Non-cardiac chest discomfort | 1 | 1 |
| Fever | 2 | 1 |
| Febrile neutropenia (related to cyclophosphamide) | 3 | 1 |

No evidence of CAR T-cell related AEs >Grade 2

- No neurotoxicity
- No cytokine release syndrome (CRS)
- No on-target, off-tumor toxicity

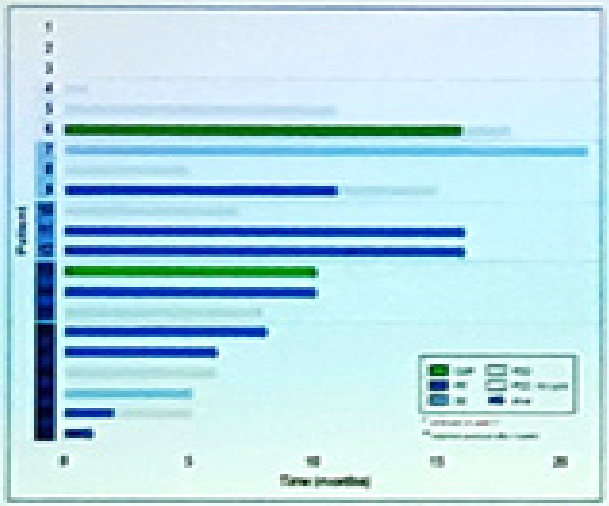
# CART Cell Mesothelioma



*Mesothelin-targeted CAR T-cell therapy*

## Clinical responses with and without addition of anti-PD-1 agent

Responses of all patients (n=21)

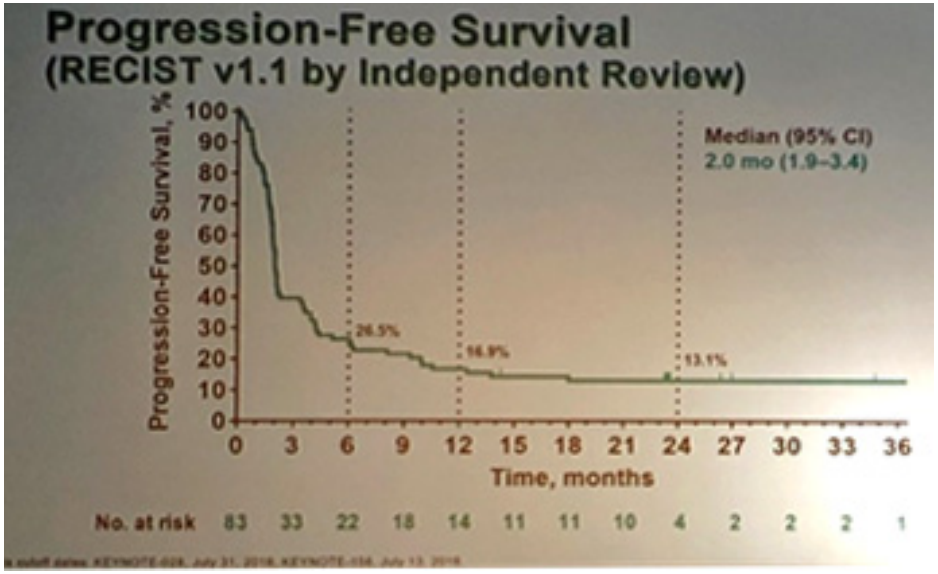


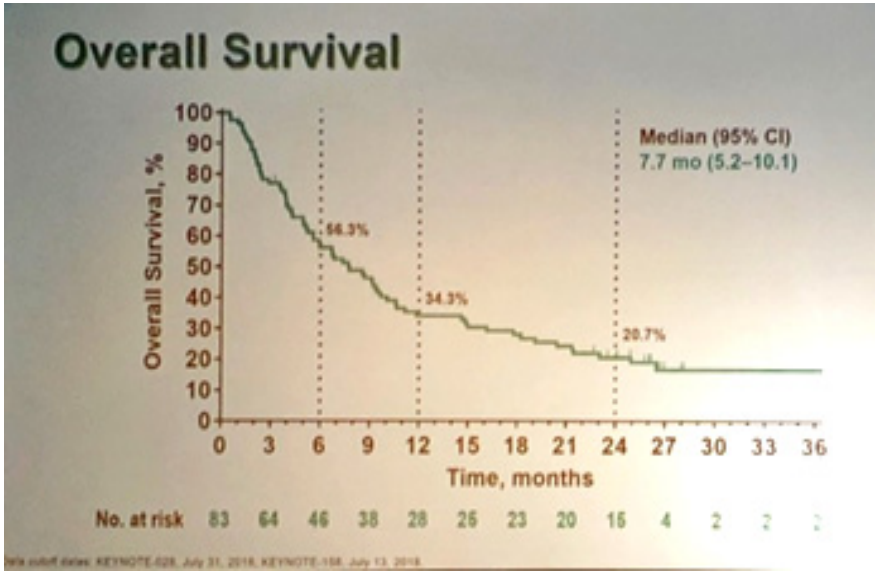
CMR – Complete metabolic response
PR – Partial response
SD – Stable disease
POD – Progression of disease

Responses of patients that received (n=11)
Cyclophosphamide and CAR T-cells and
at least 3 doses of anti-PD1 agent
with minimum 3 months follow-up

# KN28-158




Progression-Free Survival
(RECIST v1.1 by Independent Review)
Progression-Free Survival, %
Median (95% CI)
2.0 mo (1.9–3.4)
26.5%
16.9%
13.1%
Time, months
No. at risk 83 33 22 18 14 11 11 10 4 2 2 2 1


Overall Survival
Overall Survival, %
Median (95% CI)
7.7 mo (5.2–10.1)
58.3%
34.3%
20.7%
Time, months
No. at risk 83 64 46 38 28 26 23 20 15 4 2 2 2

# Efficacy of PD-1 targeted immunotherapy agents in relapsed SCLC

| | Median PFS (Months) | 1-year PFS rate (%) | Median OS (months) | 1-year OS rate (%) | Remarks |
|---|---|---|---|---|---|
| **2L(+)** | | | | | |
| **Atezolizumab** IFCT-1603 | 1.4 | <6.3 | 11.4 | 42.5 | Platinum sensitive only |
| **Pembrolizumab**/Keynote 028 | 1.9 | 23.8 | 9.7 | 37.7 | PD-L1 (+) only |
| **Pembrolizumab**/Keynote 158 | 2.0 | 23.7 | 8.7 | 40.2 | Unselected |
| **Nivolumab**/Checkmate 032 | 1.4 | 11 | 4.1 | 27 | Unselected |
| **3L(+)** | | | | | |
| **Durvalumab**/Goldman et al. | 1.5 | 14 | 4.8 | 28 | Unselected |
| **Nivolumab**/Checkmate 032 | 1.4 | 19 | 5.6 | 28.3 | Unselected |
| **Pembrolizumab/Current Study** | **2.0** | **16.9** | **7.7** | **34.3** | **PD-L1+/-** |

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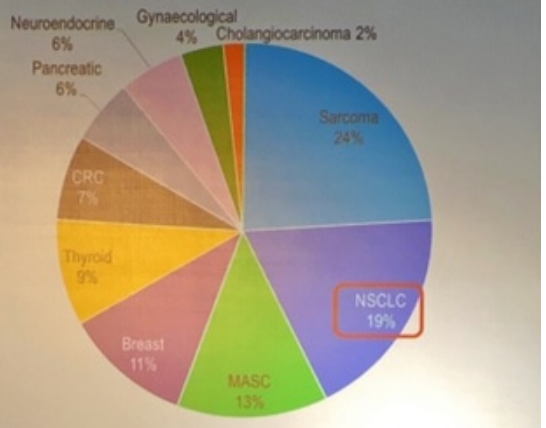
# STARTRK-2/STARTRK1-/ALKA-372-001



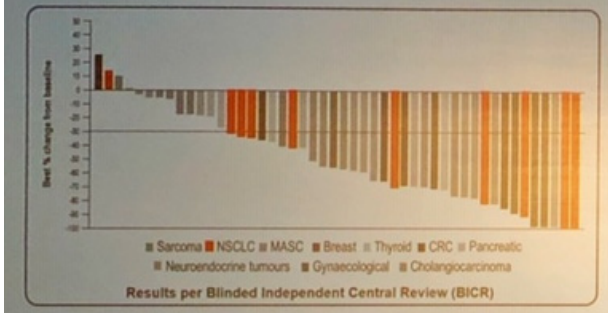
## Baseline characteristics: adult patients with *NTRK* fusion-positive solid tumors

| Baseline characteristics | | *NTRK*+ patients (n=54) | *NTRK*+ NSCLC patients (n=10) |
|---|---|---|---|
| Age, years | Median (range) | 57.5 (21–83) | 62.5 (46–76) |
| Sex, % | Female | 59.3 | 50.0 |
| | Male | 40.7 | 50.0 |
| Race, % | White | 79.6 | 70.0 |
| | Asian | 13.0 | 30.0 |
| ECOG PS, % | 0 | 42.6 | 30.0 |
| | 1 | 46.3 | 50.0 |
| | 2 | 11.1 | 20.0 |
| Prior lines of systemic therapy, % | 0 | 37.0 | 30.0 |
| | 1 | 20.4 | 30.0 |
| | ≥2 | 42.6 | 40.0 |
| CNS mets at baseline, % | | 22.2 | 60.0 |




Data cut-off date: 31 May 2018
CRC: colorectal cancer; ECOG PS: Eastern Cooperative Oncology Group performance status
MASC: mammary analogue secretory carcinoma; NSCLC: non-small cell lung cancer

## Entrectinib activity in *NTRK* fusion-positive solid tumors: individual patient responses by tumor type




| Efficacy outcomes | *NTRK*+ patients (n=54) | *NTRK*+ NSCLC patients (n=10) |
|---|---|---|
| ORR*, % (95% CI) | **57.4** (43.2–70.8) | **70.0** (34.75–93.33) |
| CR* n (%) | 4 (7.4) | 1 (10.0) |
| Median DoR,* months (95% CI) | 10.4 (7.1–NR) | NE (10.4–NE) |
| Median PFS,* months (95% CI) | 11.2 (8.0–14.9) | 14.9 (4.7–NE) |
| Median OS, months (95% CI) | 20.9 (14.9–NR) | NE (5.9–NE) |

Data cut-off date: 31 May 2018 *By blinded independent central review
Note: Patients (n=6) without matched pre/post therapy scans were excluded from the plot

CI: confidence interval; CR: complete response; CRC: colorectal cancer; DoR: duration of response
MASC: mammary analogue secretory carcinoma; NE: not estimable; NSCLC: non-small cell lung cancer
ORR: overall response rate; OS: overall survival; PD: progressive disease; PFS: progression-free survival