
SPEAR-heading
TCR
Adaptimmune
TRANSFORMING T CELL THERAPY
Elliot Norry, CMO
SITC 2020 - SURPASS poster

Disclaimer

This presentation contains “forward-looking statements,” as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), which statements may be identified by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect” and other words of similar meaning. These forward-looking statements involve certain risks and uncertainties. Such risks and uncertainties could cause our actual results to differ materially from those indicated by such forward-looking statements, and include, without limitation: the success, cost and timing of our product development activities and clinical trials; our ability to submit an IND and successfully advance our technology platform to improve the safety and effectiveness of our existing TCR therapeutic candidates; the rate and degree of market acceptance of T-cell therapy generally and of our TCR therapeutic candidates; government regulation and approval, including, but not limited to, the expected regulatory approval timelines for TCR therapeutic candidates; and our ability to protect our proprietary technology and enforce our intellectual property rights; amongst others. For a further description of the risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements, as well as risks relating to our business in general, we refer you to our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 5, 2020 and our other SEC filings.

We urge you to consider these factors carefully in evaluating the forward-looking statements herein and you are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement. The forward-looking statements contained in this presentation speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances.

We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA.

Two RECIST responses and encouraging antitumor activity

Data support future investigation of this product

Safety

- Most adverse events were consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or cancer immunotherapy

Active product

- ***Two RECIST responses*** in EGJ and head and neck cancers
- Initial ***tumor reductions*** in 5 out of 6 patients

Next steps

- ***Focus*** on patients with gastroesophageal, head and neck, lung, and bladder cancers based on data to-date
- ***Planned Phase 2 trial*** in gastroesophageal cancers (2021)

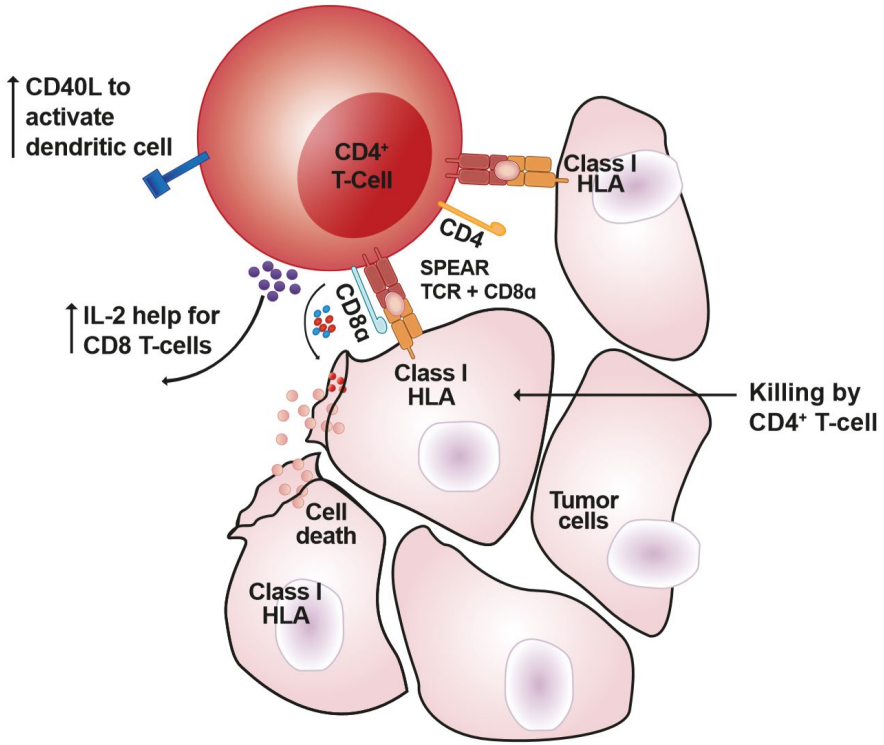
Data cut-off October 1, 2020
EGJ=esophagogastric junction cancer

BACKGROUND – SURPASS trial with ADP-A2M4CD8

A next generation SPEAR T-cell designed to improve antitumor responses

- Safety and efficacy of next-generation ADP-A2M4CD8 SPEAR T-cells
- ADP-A2M4CD8 co-expresses CD8α with ADP-A2M4 to increase the potency of CD4+ T-cells
- Given responses and antitumor activity observed with TCRs targeting MAGE-A4
  - Phase 2 trial in gastroesophageal cancers (2021)
  - Focusing SURPASS on enrolling patients with:
    - Gastroesophageal cancers (gastric, esophageal, and esophagogastric)
    - Head and neck squamous cell carcinoma (HNSCC)
    - Lung cancer
    - Bladder cancer

CD4+ T-cells stabilized by CD8α to enable killing while maintaining helper function



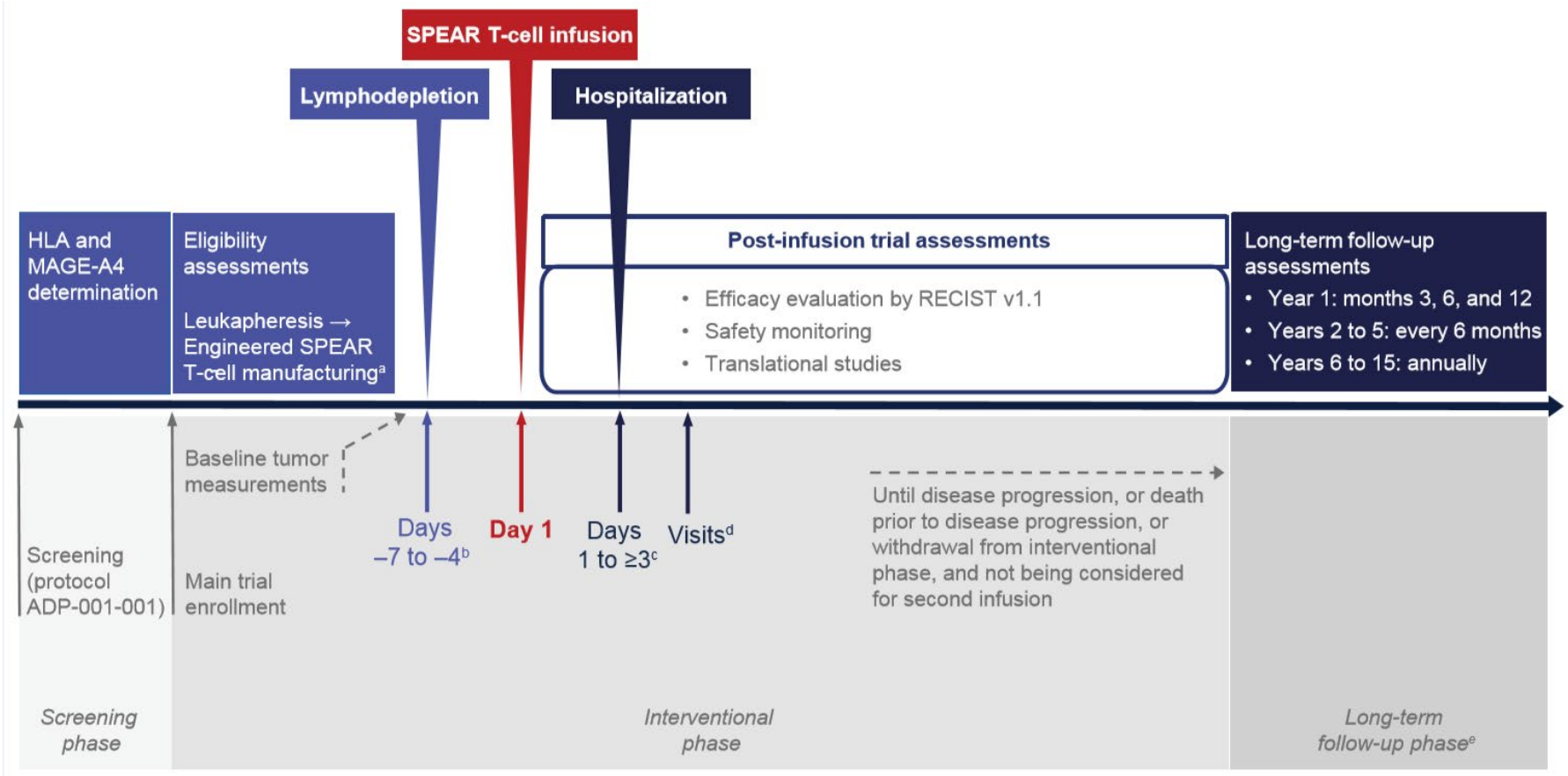
SURPASS trial design

- First-in-human dose-escalation trial using a modified 3+3 design
- First two dose cohorts (n=6 as of data cut-off)
  - Stagger between treating patients for safety evaluations
- Expansion phase
  - No stagger between patients
- DLTs adjudicated by Safety Review Committee, regardless of investigator's attribution

Cohort	Number of patients	Transduced cell doses
1	3-6	1×10^9 (range $0.8–1.2 \times 10^9$)
2	3-6	5×10^9 (range $1.2–6.0 \times 10^9$)
Expansion	Up to 30*	$1.2–10 \times 10^9$

*Includes dose escalation

SURPASS trial design schema



a) T-cell selection; lentiviral gene transfer of affinity-enhanced TCR; T-cell expansion
b) Lymphodepletion with fludarabine 30 mg/m^2/day for 4 days and cyclophosphamide 600 mg/m^2/day for 3 days
c) Hospitalization for T-cell infusion for minimum of 3 days, and discharged at Investigator's discretion
d) Days 2 to 5, 8; Weeks 2 to 6, 8, 10, 12, 18, and 24; then every 3 months until Year 2; then every 6 months
e) Up to 15 years following SPEAR T-cell infusion (Day 1)

Patient characteristics

From initial dose escalation cohorts

Characteristic	N=6
Sex; n (%) Male Female	 4 (67) 2 (33)
Median age, years (range)	58.5 (31-71)
Race, n (%) White	 6 (100)
Cancer type, n (%) EGJ MRCLS Ovarian HNSCC Esophageal	 2 (33) 1 (17) 1 (17) 1 (17) 1 (17)
ECOG performance status, n (%) 0 1	 2 (33) 4 (67)
Prior lines of systemic therapy, median (range)	3 (3-5)

ADP-A2M4CD8 safety profile in Cohorts 1 and 2

Any adverse event in more than one patient

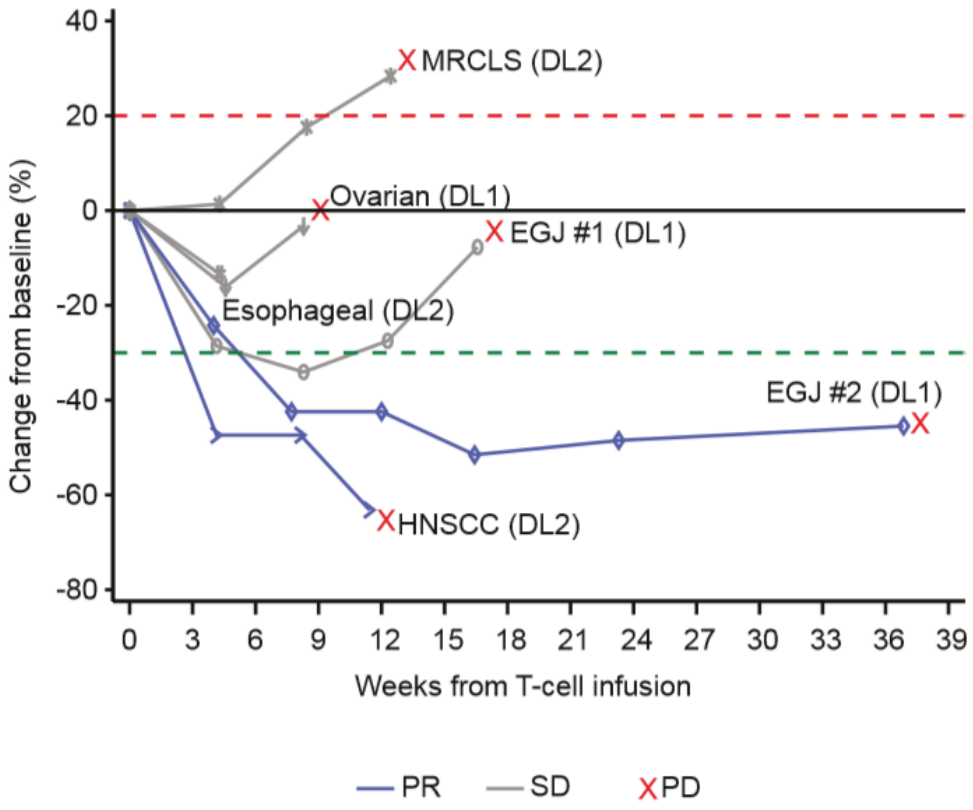
Term	Any grade, n (%)	Grade ≥3, n (%)[a]
Patients with any AEs	6 (100)	6 (100)
Leukopenia	6 (100)	5 (83)
Lymphopenia/ lymphocyte decreased	6 (100)	6 (100)
Neutropenia/ neutrophil decreased	6 (100)	6 (100)
Anemia / red blood cell decreased	4 (67)	3 (50)
Cytokine release syndrome	4 (67)	0
Fatigue	4 (67)	0
Headache	4 (67)	0
Nausea	4 (67)	0
Decreased appetite	3 (50)	0
Alopecia	2 (33)	0
Dyspnea	2 (33)	0
Hypocalcemia	2 (33)	0
Hypomagnesemia	2 (33)	0
Hyponatremia	2 (33)	2 (33)
Hypophosphatemia	2 (33)	1 (17)
Thrombocytopenia/ platelets decreased	2 (33)	2 (33)
Weight decreased	2 (33)	0

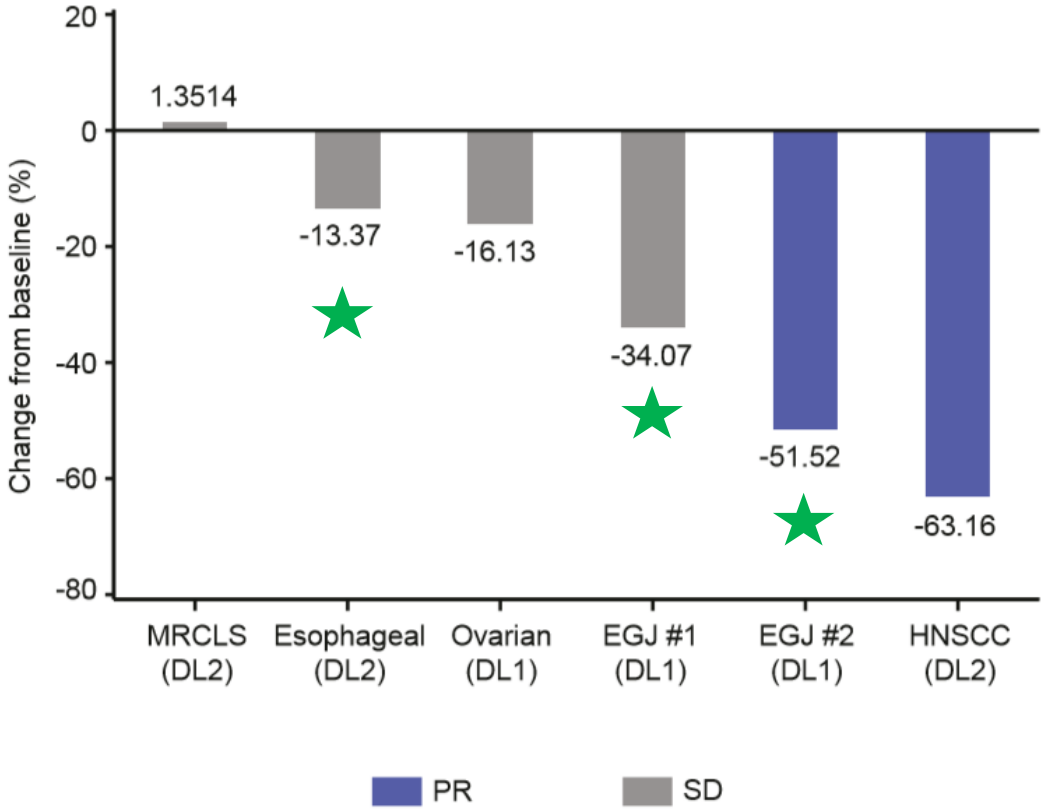
Safety (data cut-off October 1, 2020)

- Most adverse events were consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or cancer immunotherapy
- One SAE reported in a patient in Cohort 2 who had cytokine release syndrome considered to be related to T-cell infusion

Two RECIST responses and initial tumor shrinkage in five out of six patients

Promising efficacy in gastroesophageal cancers with a Phase 2 trial planned for 2021



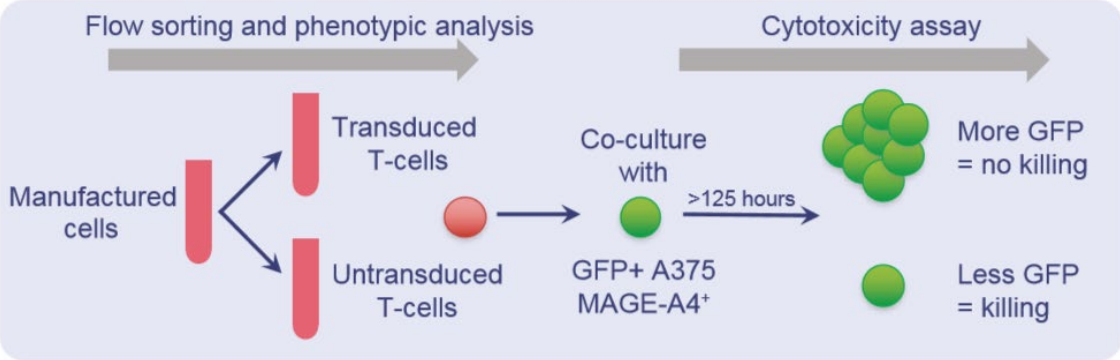


Data represent percent changes from Baseline in sum of diameters in target lesions through progression or prior to surgical resection;
Sum of diameters = sum of the long diameters for non-nodal lesions and short axis for nodal lesions;
Reponses evaluated by RECIST v1.1

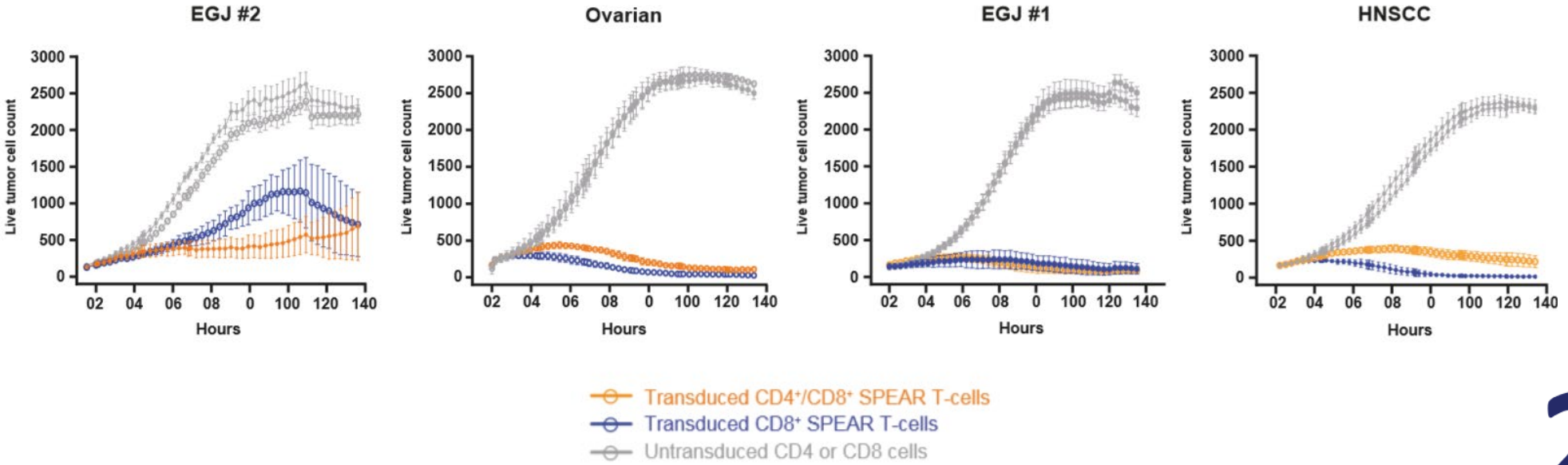
PD, progressive disease; PR, partial response; SD, stable disease

Co-expressing CD8α enables CD4⁺ cells to kill MAGE-A4 expressing target cells *in vitro*

Analyses of manufactured product from four patients in SURPASS trial



CD4⁺ T-cells expressing CD8α kill MAGE-A4⁺ target cells in vitro as well as CD8⁺ T-cells



Conclusions

Two confirmed RECIST responses and initial tumor shrinkage in five out of six patients

- **Safety**
  - Most adverse events were consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or cancer immunotherapy
- **Efficacy**
  - ***Two RECIST responses*** one in a patient with EGJ cancer; one in a patient with head and neck cancer
  - Five of six patients demonstrated initial ***tumor shrinkage***
  - Waterfall plot supports ADP-A2M4CD8 as an active product
  - Analyses of the manufactured product show that CD8 co-expression could improve $CD4^+$ T-cell potency
- **Next steps**
  - SURPASS is focused on enrolling patients with gastroesophageal, head and neck, lung, and bladder cancers
  - Phase 2 trial planned for 2021 with ADP-A2M4CD8 in patients with gastroesophageal cancers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