Novartis AG
Investor Relations

Novartis R&D Day

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NOVARTIS | Reimagining Medicine

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Iscalimab
(CFZ533)

Fully human monoclonal antibody blocking the CD154-CD40 pathway

Key highlights

Potential to provide *“One Transplant for Life”* with improved patient and graft survival and become the new SoC in transplant

Kidney transplant grafts showed pristine histology, suggesting potential to provide calcineurin-free therapy, prolonged graft survival and fewer side effects

Positive proof-of-concept study in Sjögren's syndrome, the second most common rheumatic autoimmune disease after rheumatoid arthritis

Phase 2b studies in kidney transplant and Sjögren’s on track to read out in 2021; Phase 2a readouts in systemic lupus erythematosus, lupus nephritis and hidradenitis suppurativa expected in 2021

Iscalimab blocks CD154-CD40 pathway with broad potential in multiple diseases

Alloreactivity (cellular and humoral)

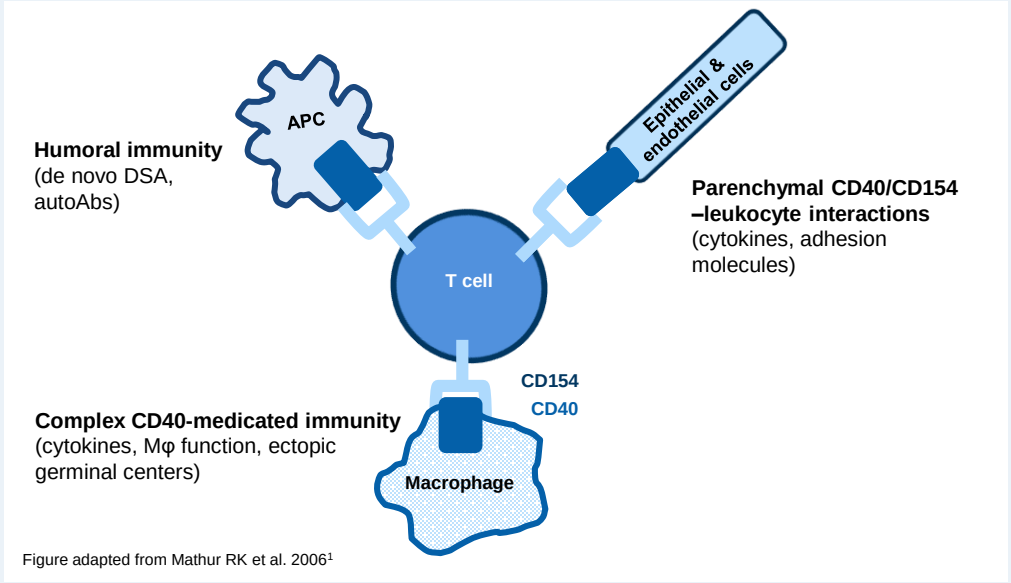


Figure adapted from Mathur RK et al. 2006[1]

CD40 (48 kDa membrane bound; ~20 kDa soluble form)[2]

- Constitutively expressed on B cells and APCs (e.g. monocytes, macrophages, dendritic cells)
- Expressed on platelets, and under certain conditions on eosinophils and parenchymal cells

CD154 (CD40 ligand)

- Induced on a variety of cell types including activated T cells, platelets, and B cells

CD40-CD154 signaling[3]

- Important for germinal center function, antibody production, and humoral memory
- Regulates macrophage, dendritic cell and parenchymal cell function
- Implicated in various autoimmune diseases

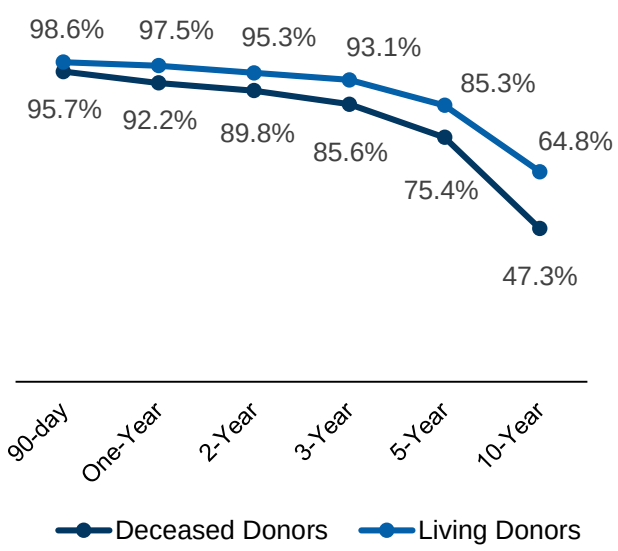
APC, antigen presenting cell; DSA, donor-specific antibodies. 1. Mathur RK, et al. Trends Parasitol. 2006;22(3):117-22. 2. Van Kooten C, Banchereau J. J Leukoc Biol. 2000;67(1):2-17. 3. Kawabe T, et al. Nagoya J. Med. Sci. 2011;73:69-78

Significant unmet need in transplantation to prolong graft survival and reduce side effects

40k+ new kidney transplant annually for an estimated 500k+ people living with a functioning kidney graft in G7 countries

2018 USRDS Annual Data Report Reference Tables, adjusted for age, sex, race, ethnicity, and primary cause of ESRD. Graft survival is determined as the earliest occurrence of either death with graft function or graft failure requiring dialysis or retransplant.

Graft survival probabilities (%)

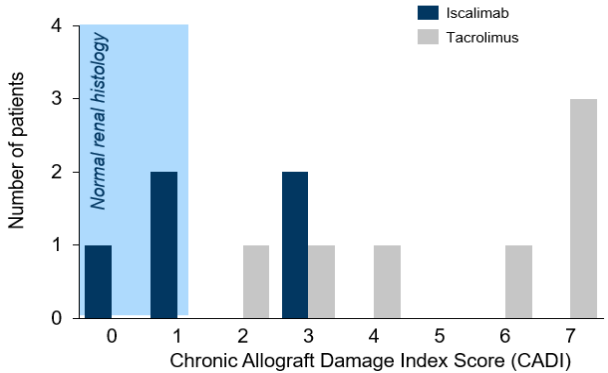


Challenges with existing Standard of Care, such as CNI-based therapies

Renal toxicity	Chronic toxicity → chronic dysfunction → return to dialysis
Cardio-metabolic complications	Frequent new-onset post-transplant diabetes, hypertension, increased cardio-vascular mortality
Insufficient graft protection	From recipient immune defense leading to progressive graft damage → return to dialysis
Cancers and infections	Cancers, bacterial and viral Infectious complications due to (over-) immunosuppression

Pristine graft histology is indicative of improved outcomes

Superior graft quality with iscalimab



Direct correlation with graft survival

- The risk for graft loss increases with the Chronic Allograft Damage Index (CADI)
- After 3 years, the graft loss is:
  - 0% for CADI 0-1
  - 5% for CADI 2-4
  - 17% for CADI >4

Yilmaz et al 2003, J Am Soc Nephrol 14: 773-779

Graft biopsies are included in two ongoing Ph2b trials:

- CIRRUS I – in kidney transplant patients (recruiting ahead of schedule); results expected H1 2021
- CONTRAIL I – in liver transplant patients (started in October 2019); results expected H2 2022

ClinicalTrials.gov, NCT02217410 (completed). Nashan et al, Am Transplant Congress 2018. Farkash et al, Am Transplant Congress 2019.

Potential to reimagine transplantion with better graft protection and less toxicity

Today with Standard of Care

10 YEARS

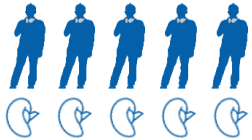
† † Death

10y median graft survival time

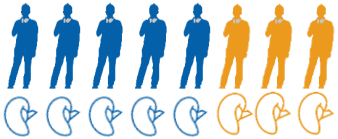
Patients return to dialysis: poor QoL and high 5y mortality (53%)

Re-transplant with another kidney, depletes pool of donor organs

Tomorrow with iscalimab



20 YEARS

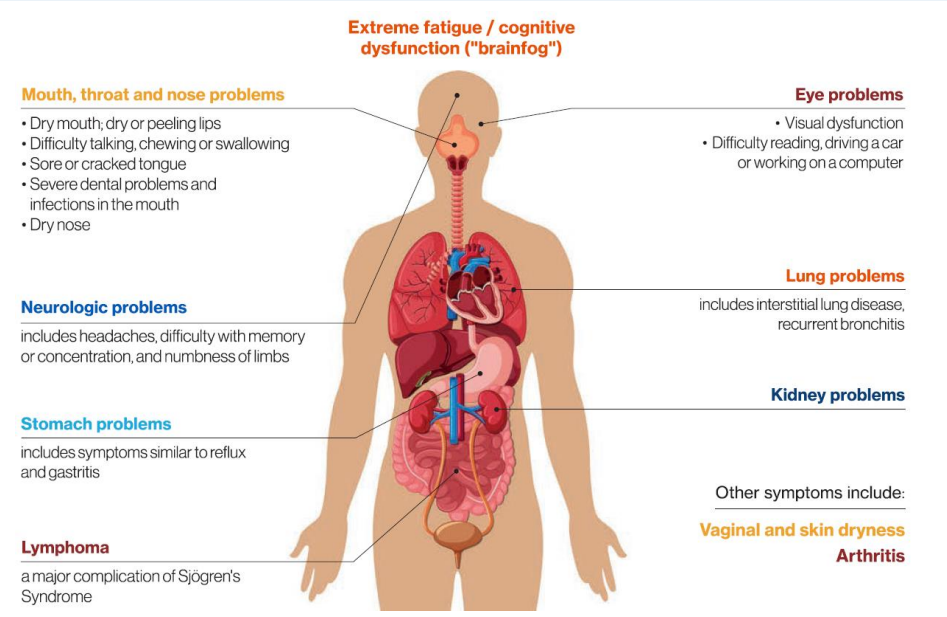


20y median graft survival time
No patients return to dialysis

Organ pool used for new patients (no re-transplantation required)

- Hypothetical illustration with a median graft survival of 20 years vs current 10-year graft survival rate at 47.3% for deceased donors in the USA (USRDS report 2018)
- Graft survival is determined as the earliest occurrence of either death with graft function or graft failure requiring dialysis or re-transplant

Sjögren's syndrome and rationale for CD40 as a therapeutic target



Prevalence and treatment

- 2nd most common autoimmune disease after RA; prevalence in adult population 0.4%
- No cure or systemic treatment approved

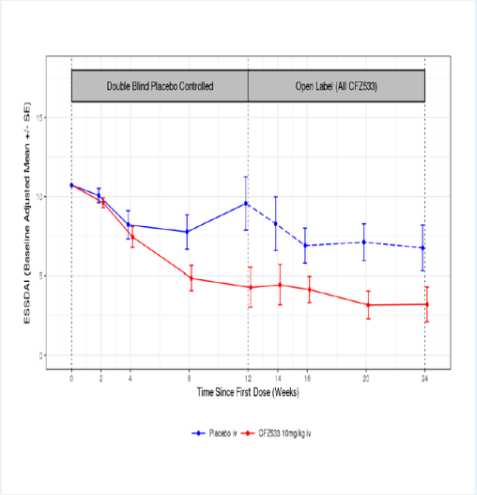
Rationale for iscalimab

- A hallmark diagnostic feature of Sjögren's syndrome is B-cell hyperreactivity
- T-cells and B-cells infiltrate patients' salivary glands and upregulate CD40 and CD154
- Positive proof-of-concept study

Fisher et al. Abstr # 1784, Am College of Rheumatology 2017

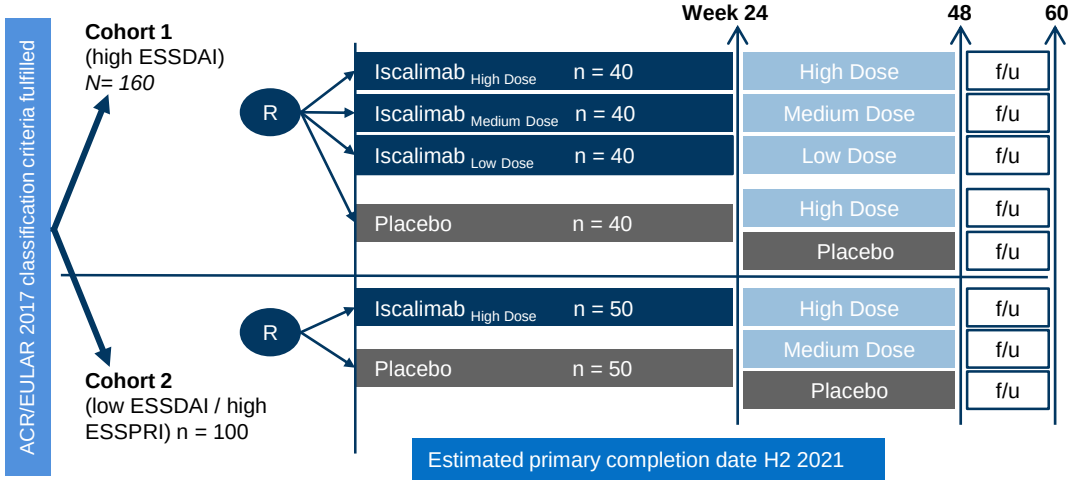
Phase 2b study in Sjögren's syndrome expected to read out in H2 2021

Positive proof-of-concept trial



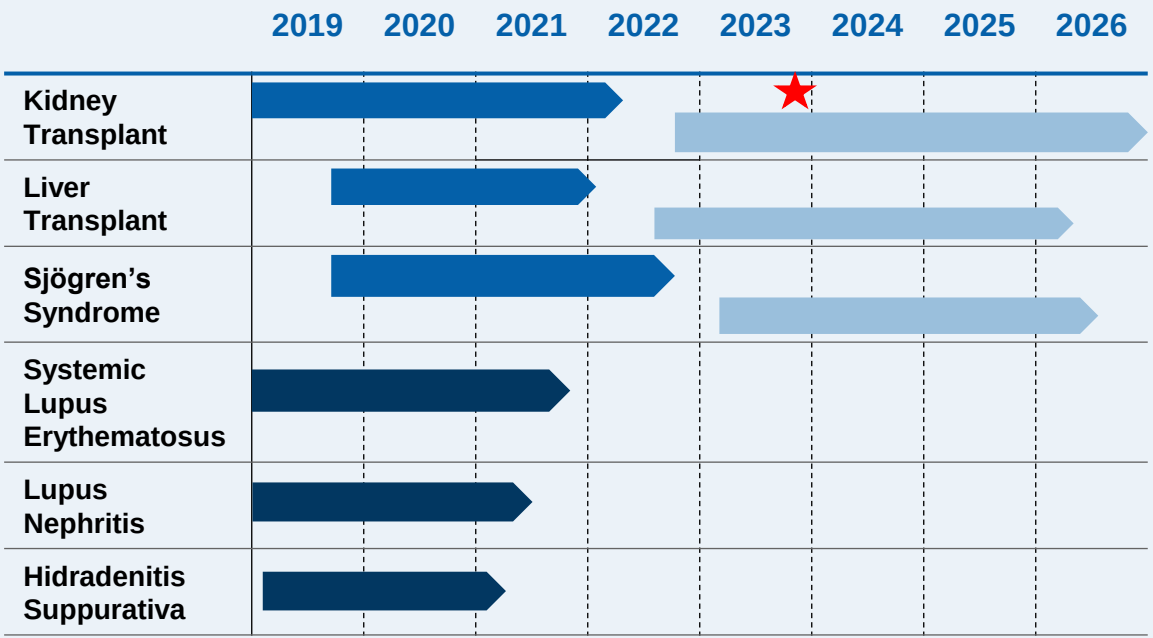
Clear improvement in CFZ533 vs placebo (mean delta = 5.6 by week 12)

TWINSS



A 48-week, 6-arm, randomized, double-blind, placebo-controlled multicenter trial to assess the safety and efficacy of multiple CFZ533 doses administered subcutaneously in two distinct populations of patients with Sjögren's Syndrome

Advancing iscalimab in a range of indications through 2020-26



- Phase 2b study in Kidney Transplantation to support early registration and conditional approval
- Anticipated launch ★ in 2023 with projected blockbuster sales potential
- Additional indications under consideration

Phase 2a
Phase 2b
Phase 3

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