CAR T Cell Therapies: Challenges and opportunities

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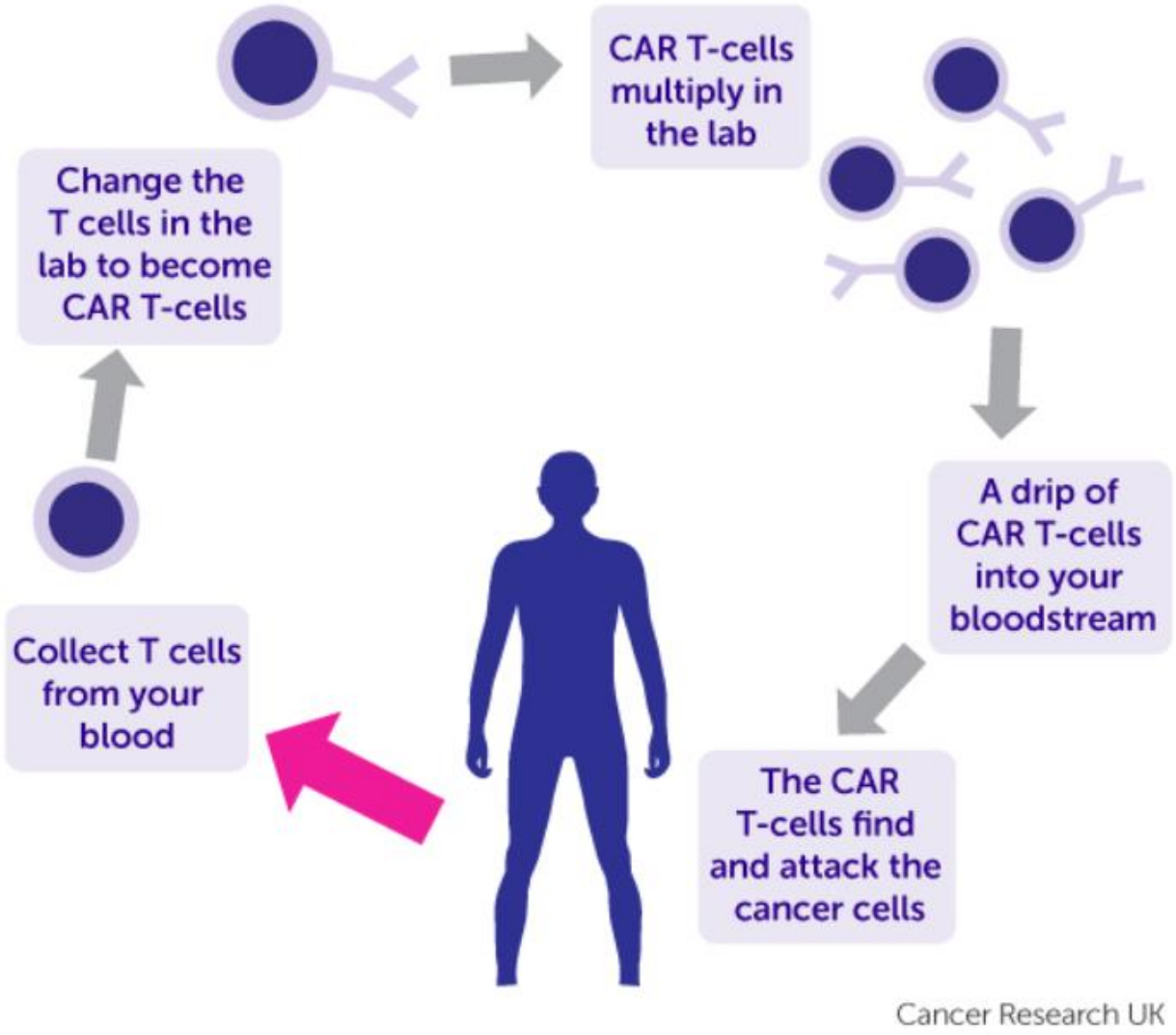
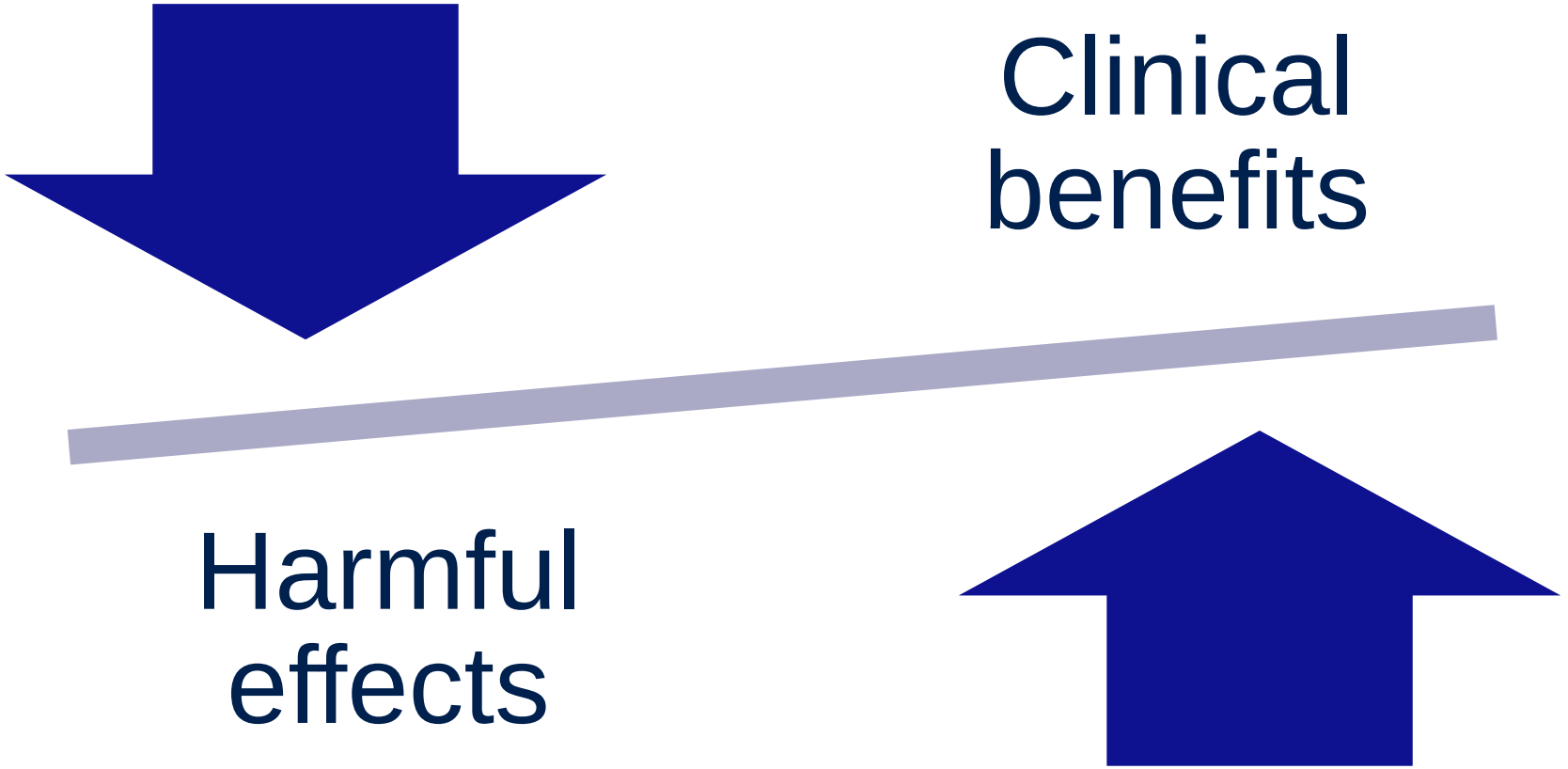
CAR T Cells

Schemata



Single treatment’s benefit-risk balance



CAR-T Cell Therapies : Development Challenges

- Manufacture quality control
- Efficacy and quality assessment
- Safety assessment
- Patient access

Autologous vs Allogeneic cells

Headline News

FDA NEWS RELEASE

FDA approval brings first gene therapy to the United States

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For Immediate Release: August 30, 2017

FDA NEWS RELEASE

FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma

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For Immediate Release: October 18, 2017

CAR-T comes to Europe: receive EU approvals

Today, the National Institute for Health and Care Excellence (NICE) has approved the use of axicabtagene ciloleucel (brand name Yescarta) to be funded for use on the NHS in England. It will be available for patients with diffuse large B-cell lymphoma (DLBCL) and primary mestinal B-cell lymphoma (PMBL), after they have tried two other systemic therapies.

Novartis-NICE deal makes Kymriah available to UK patients

By Maggie Lynch

06-Feb-2019 - Last updated on 16-Aug-2019 at 18:26 GMT

December 16, 2020

Kite's Tecartus™ (KTE-X19) Granted Conditional Marketing Authorization for the Treatment of Relapsed or Refractory Mantle Cell Lymphoma in Europe

-- 93 Percent of Patients in ZUMA-2 Pivotal Trial Responded to Single Infusion of Tecartus --

-- Tecartus is First CAR T Therapy in Relapsed or Refractory MCL and Kite Becomes the First Company with Multiple Approved Cell Therapies in Europe --

CAR-T Cell Therapies: Approval challenges

Papadouli I, Mueller-Berghaus J, Beuneu C, et al. “EMA Review of Axicabtagene Ciloleucel (Yescarta) for the Treatment of Diffuse Large B-Cell Lymphoma”, Oncologist. 2020 Oct;25(10):894-902

Sahra Ali, Rune Kjeken, Christiane Niederlaender, Greg Markey, et al. “The European Medicines Agency Review of Kymriah (Tisagenleclucel) for the treatment of Acute Lymphoblastic Leukemia and Diffuse Large B-Cell Lymphoma”, Oncologist. 2020 Feb; 25(2): e321–e327.

Andrew R. Exley, Khadija Rantell, James McBlane. “Clinical development of cell therapies for cancer: The regulators' perspective”, European Journal of Cancer, Volume 138, 2020, Pages 41-53,

CAR-T Cell Therapies: Statistical aspects: 1

Overall uncertainty:

- Significant benefit.
- Variability in product and patients.
- Small cohort size / orphan disease designation.

CAR-T Cell Therapies: Statistical aspects: 2

Estimands: (*specific quantity to be estimated in statistical analysis)*

- Treatment
- Population
- Endpoint
- Intercurrent events (e.g. use of rescue therapy)
- Population level summary

CAR-T Cell Therapies: Opportunities

- Early consideration of collaborative networks.
- Access to regulatory tools as part of ov[illegible]opment and approval strategy.
- Parallel scientific ad[illegible]pport the approval and reimbursement process.
- Use of [illegible] designs.
- [illegible]e of registries and Real-World Evidence/Data as supplementary data.

Discussion between regulator and developer may bring products to patients sooner.

Regulator ⟷ Developer

Final Remarks

- Randomised, controlled trials remain the standard for comparative evaluations.
- Registry based evaluations can be useful in situations where randomised trials are not feasible. Incorporation of existing and relevant data must be pre-specified.
- Consider the place of cell therapy within existing treatment regimen.
- Define appropriate Estimands and perform sensitivity analyses.
- Engage early in the development with patients/patient representatives and regulators.

Regulator ⟷ Developer

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Thank You

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