Patients' considerations to participate in SATs & treatments based on SAT evidence

ON HOW PATIENTS DECIDE

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Content

- My personal history with Christmas' disease/ Haemophilia B
- Personal experiences in (experimental) treatments and gene therapy
- Why patients decide (**not**) to participate in gene therapy (SAT)
- Charcteristics of Haemophilia B and gene therapy (GT)
- Relevance of patients' considerations for other SAT's

Disclosures: Advisory fees from CSL-Behring for presentations and advisory boards

My personal experiences with chronic disease

Born in 1972

Severe Haemophilia B

ABR 15-20

Hepatitis C late 70's

HIV negative

Factor replacement therapy

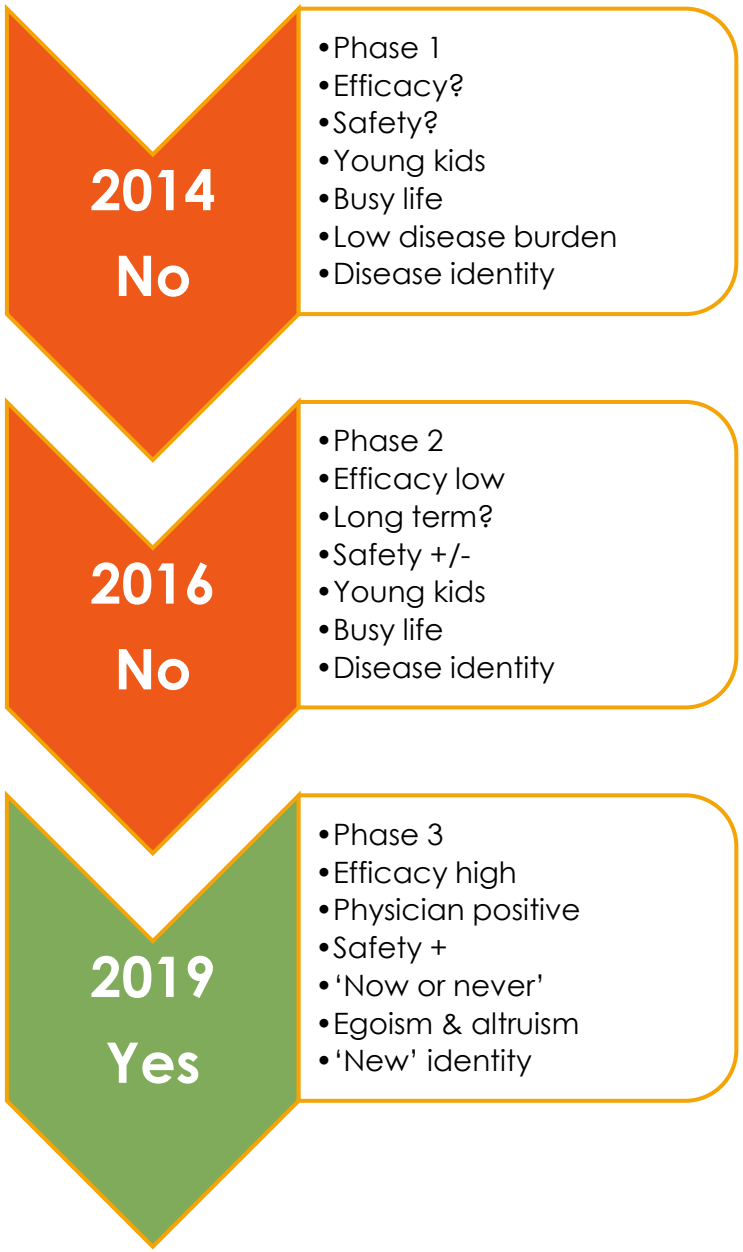
Home treatment

Personal experiences with SAT (or equivalent)

- 1982-1985: Product changes during HIV pandemic
- 1993: Interferon alfa for chronic HepC; 6 months; no remission
- 1997-1998: High dose Interferon alfa 1,5Y; in remission
- 2019: Gene therapy SAT; AAV/ Padua

“Would I take gene therapy?”

My personal decision making process



Studies on patient perspectives: participating (or not) in HemB GT

'Patient perspectives on novel treatments in Haemophilia: A qualitatative study'

Van Balen et al., The Patient, 2019

14 Dutch HemA and HemB patients

Semi structured interviews

Focus on barriers an facilitators for engaging novel therapies, amongst which GT

'The experiences of people with haemophilia and their families of gene therapy in a clinical trial setting: regaining control, the Exigency study'

Fletcher et al., OrphJRareDis, 2022

16 HemA and HemB Patients

Qualitative interviews

Focus on experiences before and after GT

'An exploration of why men with severe haemophilia might not want gene therapy: The Exigency study'

Fletcher et al., Haemophilia, 2021

12 HemA and HemB Patients

Qualitative interviews

Focus on reasons NOT to participate in GT study

Pros and cons of entering HemB GT trial

Facilitators

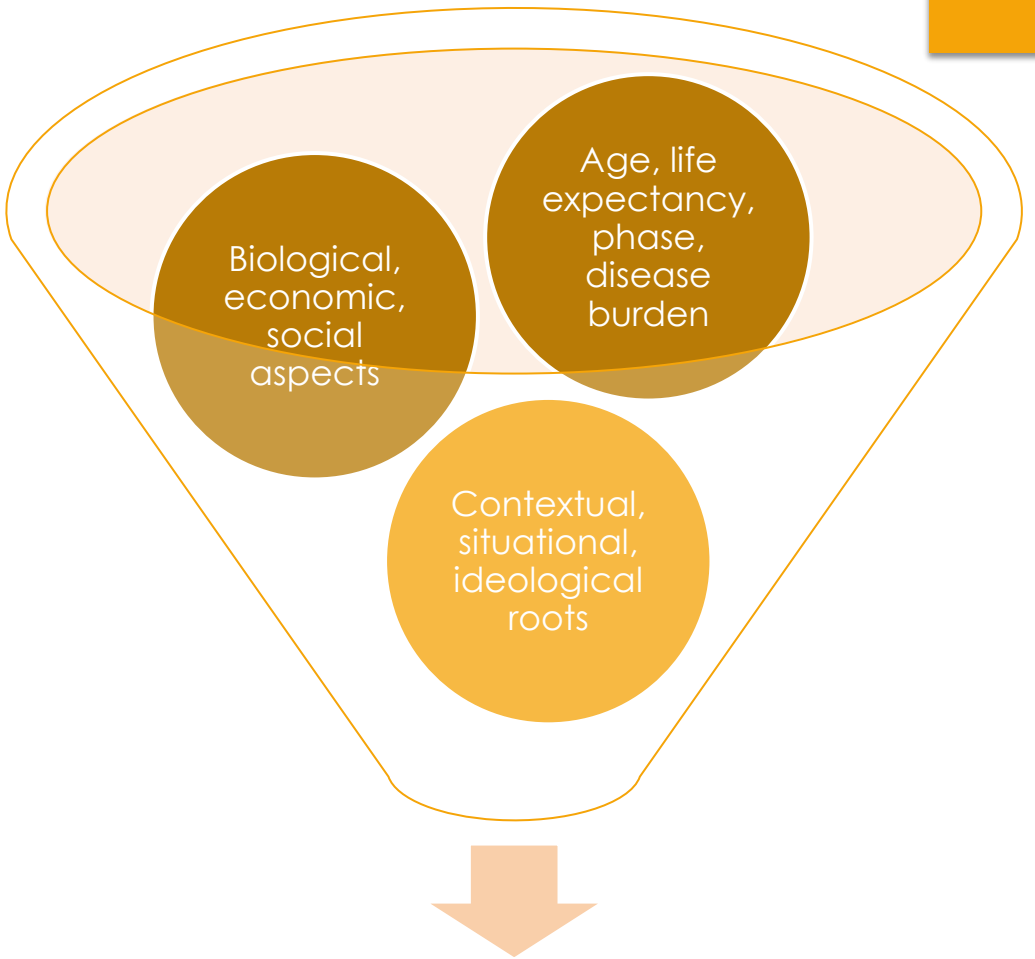
- Ease of use of the (new) medication
- Equal or better bleed prevention
- High disease/ treatment burden
- Altruism

Barriers

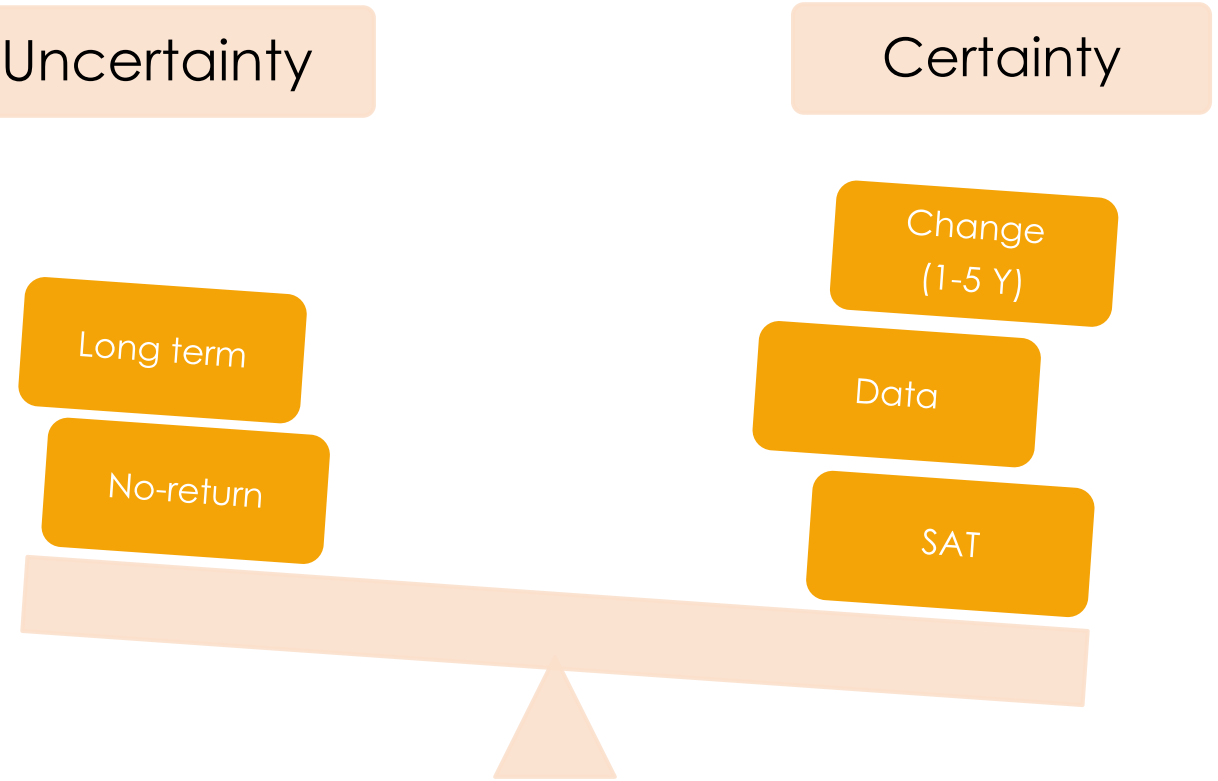
- Fear (of the unknown)
- (Long term) safety and efficacy
- Low disease/ treatment burden
- Loss of self-identity

Both altruistic and egocentric drivers motivate people to engage in gene therapy

Haemophilia Gene Therapy: Experiences and lessons from treated patients; Cedric Hermans; Orphanet Journal of rare diseases 2022



Personal pivot point



Call for RCT in Haemophilia trials

Frampton and Boudreaux

Britisch Medical Journal, May 1968

Haemostatic Factor in Peanuts

SIR,—There is need for a double-blind test for a definitive demonstration of the presence or absence of a haemostatic factor in peanuts, but we wish to emphasize certain inadequacies of the double-blind test reported by Verstraete and Ruys[1] in which they found negative results. This is to avoid any possible impression that the issue is settled. Their test was based upon the assumption that their

- HemB: rare disease
- Root cause is undisputed
- Monofactorial disease
- Well described and stable disease course
- Long term experiences with replacement therapies
- Protein expression = clinical improvement (tipping point +/-5% FIX)
- Patient data: 50% well documented (HemoNed) → RWD?

Specifics of Haemophilia

- New treatment method
- Irreversible, one-off
- Well known vector (AAV)
- Extensive animal reasearch (since 1980's)
- Societal acceptance for somatic gene editing higher than for germline applications

Specifics of Gene Therapy

Ramos, Almeida and Olsson 2023; Summary for council of Europe Bioethics committee, 2020

Factors that might influence patients' preferences for SAT or RCT

Conditional

- Access to reliable data
- Comprehensive translation into proportions of risks and benefits
- Logistics and cost
- Ideally: Fair access to next best treatment

Situational

- **How does this patient make decisions?**
- **What does the patient value most?**

- Treatment burden (old and new) and safety
- Expected efficacy (on PROM's!)
- Treating physicians' attitude towards treatment
- Life expectancy
- Is the treatment (ir)reversible?

Questions?

Thank you for your attention!