HSCT in the pediatric population – the case of PID

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HSCT in the pediatric PID patient: Role

- Allogeneic HSCT is the only curative treatment for many PIDs (>30%)
- Gene therapy modified autologoust HSCT is likely to gain importance
  - Common gamma chain SCID
  - ADA SCID
  - ARTEMIS deficiency, RAG1 SCID,…
  - WAS
  - CGD

HSCT in the pediatric PID patient: Child-specific challenges

- The child and the parents: different questions, different anxieties, different expectations
- Age-specific approach needed to explain the child
- Short-term risks: increased risk of VOD, increased risk of skin toxicity etc
- Long-term effects gain importance: SCID >< adult AML: need for judicious follow-up
  - Fertility
  - Secondary cancers
  - Auto-immunity
  - Development
  - Unknowns
- Social and emotional impact: living in a hospital for months, social isolation, siblings are left isolated, need for accommodation for the family close to the hospital…

HSCT in the pediatric PID patient: PID-specific challenges

- Optimal conditioning regimens: the jury is still out : standardization would be great but:
  - Accessibility to HSCT in the first place
  - Accessability to compounds througout Europe
  - Equal reimbursements
  - Some key drugs are under trial for « broader » use
  - The importance of long-term effects on changes in conditioning
    - E.g. stem cell infusion and late effects
    - TBI
- Standardization of monitoring (swabs, stool, urine) and protective isolation, follow-up guidelines

HSCT in the pediatric PID patient: Setting up a CT: challenges

- All the challenges mentioned above
- Esp if multinational multicenter « one PI one protocol »
- Stress on long-term impact is an absolute requirement
- Invasive sampling often needed but difficult to « defend »
- Absolute need for PK and PD studies attached to protocol if new compound
- « No fault » insurance and the position of the academic CT
- Rare diseases: off-site, transport of patients, parent lodging, family disruption, tremendous social impact
- Parental concern
- Logistic concern
- Informing the pediatricians of the ongoing trils

Logistic concerns more important than estimated Contemp Clin Trials Commun. 2017 Nov 26;9:7-12. doi: 10.1016/j.conctc.2017.11.006. eCollection 2018 Mar. **Perceived barriers to pediatrician and family practitioner participation in pediatric clinical trials: Findings from the Clinical Trials Transformation Initiative.**

HSCT in the pediatric PID patient: Challenges

Local versus Centralized e.g. gene therapy trials

- Pro centralized:
  - Rare diseases
  - Center expertise
  - Minimize inter-center variation effect on trial outcome
- Contra centralized:
  - Transport of patients AND family
  - Financing transport, lodging, unemployment …
  - Tremendous social impact « isolation »
  - Follow-up visits: Who pays? How long? (ideally very long)
  - What if the patient dies? « No fault » - who pays transport?

HSCT in the pediatric PID patient: Recommendations

International guidelines on CT development (EU wide) beyond the CT

PK / PD: inclusion of children in CT should be obligatory

International agreements of Health Insurances on « standards »

Advise and facilitate on standardized long-term follow-up

Disease group specific announcements on CTs

Avoid dispersion – merge information for optimal access

Use registries better and again avoid dispersion

Attention for psycho-social impact