

Pediatric Ethics Subcommittee Meeting: Summary

December 9, 2008

General Discussion

- The PES discussed the general question of the ethics of sibling BM donation in a clinical setting. Among the issues considered was (1) whether or not a third party should be involved as an advocate for the potential donor; (2) whether the justification for parental discretion in the decision to permit BM donation from one sibling to another sibling is based on any purported benefit (whether considered direct or indirect) to the donor or on the absence of significant risk of serious harm. The PES also touched on the question of precedent, and the relationship of recommendations made during the course of deliberations today and future protocols involving healthy siblings as BM donors.

Consideration of Subpart D Categories

405 Issues:

Prospect of Direct Benefit

- Direct benefits are those that accrue directly, i.e., in a proximate manner, to the donor-subject as a result of research participation; focus of research hypothesis is effect of G-CSF
- Clinical practice: direct benefit argument has traditionally been used
- Possibility of lower BM volume being harvested pertains to future donors, not study donors

405 Issues:
Benefits Justify the Risks?

DECISION: No consensus

405 Decision

- Intervention-donors would not be in 405, because of lack of direct benefit

406 Issues:

Minor Increase over Minimal Risk

DECISION: More than minor increase:

- 2 cases of deaths from ARDS
- Even though probability is small, severity is great
- Limited information available on G-CSF

406 Issues:

Condition or Disorder

- Not a condition or disorder:
 - Not addressed in the hypothesis
 - Too much of a stretch, esp. since donors are being placed at risk by G-CSF
 - HLA type is not a condition per se
 - Being in a difficult circumstance does not rise to the level of being a condition
 - Being assigned to the intervention arm shouldn't mean the child now has a "condition"
 - Meeting an inclusion criteria (a characteristic) doesn't mean the child now has a condition

406 Issues:

Experiences Reasonably Commensurate

- “Experience” includes experience with procedures and side effects
- Main side effects are bone pain and myalgia
- G-CSF administration does not increase time in hospital

DECISION: No Consensus

406 Issues:

Vitally important knowledge

DECISION: No

406 Decisions

- Intervention-donors do not qualify

407 Issues:

Reasonable opportunity for
generalizable knowledge, in accord
with sound ethical principles

DECISION: Yes

Subpart D Approval Categories

	Control	Intervention
Donors	46.404 / 50.51	46.407 / 50.54
Recipients	46.404 / 50.51	46.405 / 50.52

Subcommittee Determinations

- 1) The research risks that should be considered when evaluating the inclusion of the healthy sibling donors is the incremental research risks of the G-CSF administration.
- 2) The risks of G-CSF administration are more than a minor increase over minimal risk. Thus the protocol cannot be approved (for the healthy sibling donors) using 21 CFR 50.51 / 45 CFR 46.404 or 21 CFR 50.53 / 45 CFR 46.406.
- 3) There are benefits to the donor (although some panel members thought these benefits somewhat speculative), but these should be considered indirect. Thus the protocol cannot be approved using 21 CFR 50.52 / 45 CFR 46.405.
- 4) The donors do not have a condition with respect to this protocol. Thus, in addition to the risk of G-CSF administration, the lack of a condition means that the inclusion of healthy sibling donors cannot be approved using 21 CFR 50.53 / 45 CFR 46.406.

Subcommittee Determinations

- 5) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
- 6) The research can be conducted in accord with sound ethical principles (with one dissenting vote), assuming the following changes (below) are made to the protocol and consent documents.
- 7) The inclusion of healthy sibling donors in this research protocol can be approved using 21 CFR 50.54 / 45 CFR 46.407.

Stipulations

- All donors with any increased risk for BM donation (not simply high risk) should be excluded. For example, the presence of an uncontrolled infection as an exclusion criterion should be altered to any child with an active infection, especially pulmonary.
- Each research site should appoint an independent person to function as an advocate for the potential sibling donor.
- Last two bullet points in the parental informed permission document (ARDS, leukemia) should indicate that they are potentially life-threatening.
- All things being equal, preference should go to an older sibling donor.

Recommendations

- None

Vote

- Nine in favor of motion with stipulations.
- Two “No” votes
 - One No Vote: Subject advocate should be a recommendation, not stipulation. Would vote in approval otherwise.
 - Second No Vote: Research not in accord with sound ethical principles.