Questions Posed by Participants

Mechanisms of Disease

1. What are the key genetic events in the pathogenesis of chordomas?
2. How does germ-line copy duplication of brachyury cause familial chordoma?
3. Are chordomas dependent on brachyury for survival?
4. What are the relevant downstream targets of brachyury?
5. What are the signaling pathways that regulate the growth and survival of chordoma?
6. What role does the tumor microenvironement play in chordoma initiation and progression?
7. Why do chordomas arise from within the bone and not the intervertebral disc? Is there some factor in the bone that causes notochordal cells to proliferate?
8. What triggers metastasis? Why do some chordomas metastasize while others do not?
9. What explains the difference in age of onset for sacral vs. clival chordomas? Are the mechanisms of pathogenesis different for sacral vs. clival chordomas?
10. Are pediatric chordomas biologically distinct from adult chordomas?
11. What explains the difference in survival based on gender? What explains the difference in anatomical distribution based on gender? Do sex hormones play a role in the initiation or progression of chordoma?

Therapeutic Development

12. Of the currently tractable drug targets, which play a role in chordoma?
13. What targeted therapies have been most effective in treating chordoma patients with advanced disease?
14. Why are chordomas resistant to cytotoxic chemotherapies?
15. Is there currently sufficient rationale to justify any clinical trials? What additional rationale would be needed?
16. Can we effectively deliver small molecules, antibodies, or imaging agents to chordoma?
17. Why do these tumors require such high radiation doses for tumor control? Can radiation sensitizers be used to increase effectiveness of radiation?

Questions Posed by Participants

Clinical Management

18. How many chordomas go undiagnosed and untreated due to lack of knowledge about the disease?

19. Does neoadjuvant radiation and/or chemotherapy improve clinical outcome?

20. Would adjuvant chemotherapy be beneficial even in cases of gross total resection?

21. What radiation total dose and dose fractionation are needed in order to treat chordomas? Is hypofractionation biologically advantageous?

22. What form of radiation is optimal – protons, carbon ions, radiosurgery?

23. Can high-dose radiation alone durably control chordoma?

24. Are there valid clinical predictors of which patients can be successfully treated with surgery alone and which require adjuvant surgery?