ORS MSKI ICM Vote

1. Do joints have a natural microbiome, and does this affect joint infection?

- Agree: 46
- Disagree: 18
- Abstain: 8

2. Does gut microbiome affect host immunity during MSKI?

- Agree: 70
- Disagree: 0
- Abstain: 2

3. Does antibiotic therapy affect host immunity to MSKI?

- Agree: 53
- Disagree: 13
- Abstain: 6
4. Are there validated models of host immunity and with quantitative outcome measures?

- Agree: 65
- Disagree: 2
- Abstain: 5

5. Are there rigorous approaches for detecting and quantifying intracellular bacterial reservoirs?

- Agree: 63
- Disagree: 7
- Abstain: 2

6. Can human immune responses be fully recapitulated in animal models of MSKI?

- Agree: 64
- Disagree: 3
- Abstain: 5

7. Does antiinflammatory medication influence MSKI in preclinical models?

- Agree: 65
- Disagree: 2
- Abstain: 5
8. Does autoimmunity affect musculoskeletal infection in animal models?

- Agree: 41
- Disagree: 7
- Abstain: 24

9. Is there an established immunization protocol (adjuvant, route of administration, time between boost) to assess novel vaccines for MSKI?

- Agree: 59
- Disagree: 4
- Abstain: 9

10. Are there interventions beyond vaccination known to boost host immunity to MSKI in animal models?

- Agree: 55
- Disagree: 7
- Abstain: 10

11. Has the immune proteome been well-defined in animal models of MSKI?

- Agree: 62
- Disagree: 3
- Abstain: 7
12. Are there vaccines/passive immunizations for MSKI in animal models? (e.g. *S. aureus*)?

- **Agree**: 64
- **Disagree**: 3
- **Abstain**: 5

13. Does prior MSKI shape immune responses to subsequent bacterial infection?

- **Agree**: 70
- **Disagree**: 0
- **Abstain**: 2

14. Is the antibody response to MSKI pathogen-specific?

- **Agree**: 69
- **Disagree**: 0
- **Abstain**: 3

15. Are certain species more susceptible and resistant to MSKI based on host immunity than others?

- **Agree**: 65
- **Disagree**: 3
- **Abstain**: 4
16. Is there a standard timeline or duration of treatment to best evaluate resolution of infection in animal models of MSKI?

- Agree: 64
- Disagree: 4
- Abstain: 4

17. Does radiography score correlate to infection and treatment efficacy for bone?

- Agree: 59
- Disagree: 6
- Abstain: 7

18. Are there any imaging techniques available that can effectively indicate the degree of infection or monitor the advancement of the disease in animal models of MSKI?

- Agree: 66
- Disagree: 2
- Abstain: 4

19. Are In Vivo Imaging Systems (IVIS) Using Fluorescence or Luminescence Complementary to Other Methods Such as Culture or PCR?

- Agree: 67
- Disagree: 3
- Abstain: 2
20. Can techniques be employed to precisely evaluate the formation of biofilms on implants or infected bone in in vivo models of osteomyelitis?

- Agree: 64
- Disagree: 1
- Abstain: 7

21. Is there an animal model representative of DAIR (debridement, antibiotics, and implant retention)?

- Agree: 60
- Disagree: 4
- Abstain: 8

22. Is there a single predominant combination of bacterial species in humans that should be studied in animal models of polymicrobial MSKI?

- Agree: 61
- Disagree: 5
- Abstain: 6

23. Are there immunological plasma biomarkers that are useful to measure infection or treatment effects in rat models of musculoskeletal infection?

- Agree: 62
- Disagree: 4
- Abstain: 6
24. Can all standard-of-care antibiotics included in the clinical treatment guidelines for musculoskeletal infection be used in animal models?

- Agree: 65
- Disagree: 2
- Abstain: 5

25. Question removed

26. Is a statistically significant reduction in bacterial burden clinically significant, if infection remains after treatment in animal models of infection?

- Agree: 50
- Disagree: 13
- Abstain: 9

27. After using an antimicrobial-loaded biomaterial in an animal study, can you prevent false negative culture results due to antimicrobial carryover during sample processing in the lab?

- Agree: 65
- Disagree: 3
- Abstain: 4
28. Should treatment of fracture and/or implant related infection always include debridement in animal models?

- Agree: 51
- Disagree: 13
- Abstain: 8

29. Should synovial biomarkers be investigated for MSKI in large animal models?

- Agree: 63
- Disagree: 1
- Abstain: 8

30. Are there any recommended diagnostics to monitor the safety of antibiotic therapy in animal models?

- Agree: 55
- Disagree: 4
- Abstain: 13

31. Do X-ray and advanced imaging have a role in diagnosing PJI using animal models?

- Agree: 62
- Disagree: 2
- Abstain: 8
32. Are there specific animal tissues that need to be studied to diagnose MSKI and treatment outcomes?

- **Agree**: 64
- **Disagree**: 1
- **Abstain**: 7

33. Are there unique pathophysiologic features of MSKI in the pediatric population?

- **Agree**: 54
- **Disagree**: 0
- **Abstain**: 18

34. Does antibiotic use in patients with periprosthetic joint infection (PJI) increase the risk of antibiotic resistance compared to the general population?

- **Agree**: 60
- **Disagree**: 8
- **Abstain**: 4

35. Are there generalizable negative and positive controls that be incorporated within all biofilm experiments to allow cross-referencing between experiments?

- **Agree**: 48
- **Disagree**: 3
- **Abstain**: 21
36. Can antibiotic tolerance be used to support the presence and maturity of a biofilm?

- Agree: 57
- Disagree: 9
- Abstain: 6

37. Can drug clearance and protein binding be modeled in an in vitro system to predict efficacy of drugs?

- Agree: 54
- Disagree: 5
- Abstain: 13

38. Can in vitro antimicrobial efficacy (CFU log 2 or log 3 reduction) be used to achieve the minimum rationale for moving into the animal?

- Agree: 62
- Disagree: 4
- Abstain: 6

39. Is there a best method for assessing MBEC in vitro?

- Agree: 59
- Disagree: 4
- Abstain: 9
40. Is there a “race for the surface” between bacteria and host cells that determines the clinical outcome of orthopaedic implant surgery?

- Agree: 42
- Disagree: 22
- Abstain: 8

41. Is a minimum 1.5 log (95%) reduction in CFU on a surface, in vitro, sufficient for minimal antibacterial activity, in vivo, using a 104-105 CFU/mL inoculum?

- Agree: 45
- Disagree: 11
- Abstain: 16

42. Does testing against a panel of *S. aureus* (MSSA and MRSA), *S. epidermidis*, GBS, *E. coli*, *P. aeruginosa*, *C. acnes* and *C. albicans* sufficiently capture the minimum required strains to claim universal antimicrobial efficacy when considering a novel prevention technology?

- Agree: 50
- Disagree: 9
- Abstain: 12

43. Should multiple outcome measures be used for accurately determining antibacterial efficacy in vitro.

- Agree: 70
- Disagree: 0
- Abstain: 2
44. Is there a universal concentration for the bacteriological tests of (1) textured surfaces, (2) eluting surfaces, and (3) non-eluting (chemically modified) surfaces?

- Agree: 61
- Disagree: 3
- Abstain: 8

45. Should Small Colony Variants orPersisters be detected in clinical samples?

- Agree: 52
- Disagree: 9
- Abstain: 11

46. Should you use the same sterilization method in vitro as you will be using in vivo?

- Agree: 67
- Disagree: 2
- Abstain: 3

47. Are there rigorous in vitro bone cell models for intracellular infection in osteomyelitis?

- Agree: 61
- Disagree: 2
- Abstain: 9
48. Is there a standard method to detach and quantify bacteria attached to surfaces?

- Agree: 59
- Disagree: 5
- Abstain: 8

49. Can existing ISTA/ASTM standards be used for constructing biofilm models on medical devices?

- Agree: 57
- Disagree: 2
- Abstain: 12

50. Should we (as the MSKI group) recommend certain models (and promote them) to have more homogenous experimental settings?

- Agree: 66
- Disagree: 3
- Abstain: 3

51. Are there specific preclinical animal models of musculoskeletal infection that are accepted by FDA and other regulatory agencies.

- Agree: 60
- Disagree: 4
- Abstain: 8
52. Are there best practice guidelines for pivotal preclinical studies supporting regulatory submissions for drugs, devices, and drug-device combination products?

- Agree: 58
- Disagree: 3
- Abstain: 11

53. Are there best practice guidelines for the duration of an antimicrobial effect from an orthopedic implant in vivo to prevent clinical infection?

- Agree: 63
- Disagree: 3
- Abstain: 6

54. Are there any effective host immune responses against biofilm bacteria?

- Agree: 46
- Disagree: 5
- Abstain: 19

55. How does host immunity against a pathogen change based on the location of the MSKI?

- Agree: 48
- Disagree: 2
- Abstain: 21
56. Are there any effective host immune responses against bacteria within the OLCN?

- Agree: 40
- Disagree: 3
- Abstain: 28

57. Do bone cells mount an immune response during MSKI?

- Agree: 42
- Disagree: 8
- Abstain: 21

58. What are the proven outcome measures of host immunity during MSKI?

- Agree: 44
- Disagree: 2
- Abstain: 24

59. Is there host immunity against small colony variants and persister cells?

- Agree: 45
- Disagree: 3
- Abstain: 22
60. What is known about antigen specific T-cells in MSKI?

61. What are the important antigen presenting cells in MSKI?

62. Is septic non-union associated with host immunity?

63. Do different pathogens influence host immunity against each other in polymicrobial MSKI?
64. Are monoclonal antibodies capable of eradicating biofilms in animal models of MSKI?

- Agree: 44
- Disagree: 7
- Abstain: 20

65. What are the best models to study T-cell responses during MSKI?

- Agree: 47
- Disagree: 1
- Abstain: 23