Summary of "ESMO 2025 Summary: Emerging Therapies in Bone Sarcoma" by Emanuela Palmerini

This video provides a comprehensive update on emerging therapies for bone sarcomas, presented at ESMO 2025. Dr. Emanuela Palmerini discusses the challenges of treating rare and heterogeneous bone tumors, including osteosarcoma, Ewing sarcoma, and chondrosarcoma, and highlights recent advancements in treatment strategies.
(Currently the video is not accessible to the general public.)

Key Topics Covered:

1. Bone Sarcoma Types and Survival Rates

- Bone sarcomas are rare, with fewer than 4,000 new cases annually in the U.S.
- Osteosarcoma (40%), Ewing sarcoma, and chondrosarcoma are the most common subtypes.
- Survival rates have improved with chemotherapy: ~80% for localized Ewing sarcoma and ~75% for osteosarcoma.
- High-risk patients benefit from mifamurtide and ifosfamide, as shown in recent studies. **[00:00]**

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2. Tumor Microenvironment in Sarcomas

- The tumor microenvironment plays a critical role in prognosis and treatment response.
- A gene signature involving immune T-cell trafficking predicts survival, with low CD8, Treg, and NK cells associated with better outcomes.
- Agents targeting the tumor microenvironment are under investigation, including mifamurtide and other immune-modulating therapies. **[01:37]**

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3. Tyrosine Kinase Inhibitors (TKIs)

- TKIs like cabozantinib, zanzalintinib, and apatinib show promise in osteosarcoma, with objective response rates up to 40%.
- Combination therapies (e.g., cabozantinib with MAP chemotherapy) are being explored in the U.S. and Europe.
- Regorafenib and lenvatinib are also being studied in combination with chemotherapy for high-risk patients. **[03:40]** **[05:10]**

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4. Promising Targets and Drug Trials

- **Ewing Sarcoma:** WEE1 inhibitors (e.g., azenosertib) and DNA damage response agents (e.g., ceralasertib, PARP inhibitors) are under investigation.
- **Osteosarcoma:** MYC amplification is a negative prognostic factor, and new agents targeting MYC are in development.
- **Chondrosarcoma:** IDH1/2 inhibitors (e.g., ivosidenib) and INBRX-109 (targeting TRAIL receptors) show encouraging results in clinical trials. [06:54] [20:03]

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5. Immunotherapies and Checkpoint Inhibitors

- Immune checkpoint inhibitors (e.g., nivolumab, sunitinib) show partial responses in differentiated chondrosarcoma and osteosarcoma.
- Novel surface-targeted agents (e.g., HER2, GD2, B7-H3) and antibody-drug conjugates are being developed.
- CAR-T therapies targeting GD2 and B7-H3 are promising but require better patient selection and biomarkers. [09:19] [12:59]

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6. Emerging CAR-T and Novel Agents

- CAR-T therapies targeting HER2 and ephrin-B2 show potential, with some complete responses in osteosarcoma.
- Novel agents like folate receptor-alpha inhibitors and leucine-rich repeat proteins are in early trials.
- Immunotheranostics and radio-labeled agents are being explored for targeted delivery. [19:46]

Conclusion

Dr. Palmerini emphasizes the progress made in the last five years, particularly in chondrosarcoma and osteosarcoma, with promising new agents and combination therapies. She highlights the importance of collaboration, biomarker development, and attention to detail in advancing bone sarcoma research.