GU Cancers Live Chat Summary

Best of Kidney Cancer 2024 - Dr. Wenxin (Vincent) Xu

Key Takeaways:

- Adjuvant Immunotherapy in RCC:
    - The role of adjuvant immunotherapy continues to evolve, with pembrolizumab showing an overall survival (OS) benefit.
    - Patient selection remains crucial, as many patients receiving adjuvant therapy might be cured with surgery alone.
    - Biomarkers such as KIM-1 could help identify patients who may safely skip adjuvant therapy versus those who would derive maximum benefit.

- Post-ICI Treatment Strategies:
    - Results from TiNivo-2 and CONTACT-03 emphasize the limitations of sequential ICI-based therapies in RCC.
    - The findings highlight the need for biomarker-driven treatment approaches to address resistance mechanisms and optimize sequential therapies.
    - Potential alternative strategies include VEGF blockade and HIF-2 inhibitors in the refractory setting.

- Predictive Biomarkers & Future Directions:
    - Transcriptomic analyses and mRNA signatures offer promise in guiding treatment decisions.
    - Trials such as OPTIC-RCC are exploring the use of baseline mRNA signatures for treatment selection.
    - However, implementation in clinical practice remains challenging due to availability, turnaround time, and standardization.

Discussion Highlights:

- Evolving Landscape of Adjuvant Therapy:
    - The future of adjuvant therapy may involve combination approaches (e.g., pembrolizumab + belzutifan or mRNA vaccines).

- Overcoming Resistance in Sequential Therapy:
    - CONTACT-03 and TiNivo-2 findings suggest that PD-1/PD-L1 rechallenge should be biologically informed rather than used indiscriminately.
    - Emerging biomarkers (mRNA, epigenetic signatures) may help identify patients likely to respond to alternative targeted therapies.

- Challenges in Biomarker Integration:
    - Scalability and accessibility of mRNA-based biomarkers remain major barriers.
    - The field is exploring proxy biomarkers that could provide clinically actionable insights without requiring complex transcriptomic analyses.

Conclusion:

Dr. Xu's presentation underscored the growing role of immunotherapy and biomarker-driven approaches in RCC. While adjuvant therapy continues to expand, refining patient selection and addressing post-ICI treatment resistance will be critical in optimizing outcomes. The integration of biomarkers remains a key challenge but holds promise in shaping the future of personalized treatment strategies in RCC.

Prostate Cancer – Dr. Silke Gillessen

Key Takeaways:

- Ultra-Hypofractionation in Localized Prostate Cancer:
    - PACE-B trial confirms stereotactic body radiotherapy (SBRT) as an effective and well-tolerated option for intermediate-risk prostate cancer.
    - While long-term data beyond 5 years are still needed, current results are encouraging.
    - Low-risk patients should still be managed with active surveillance rather than immediate radiation.

- Treatment Intensification in Low-Volume mHSPC:
    - Abiraterone ± docetaxel combined with radiotherapy (RT) shows additional benefits in de novo metastatic hormone-sensitive prostate cancer (mHSPC).
    - RT benefits were observed specifically in patients also receiving abiraterone, reinforcing the importance of multimodal treatment in select patients.
    - The role of RT in high-volume mHSPC remains under investigation, with potential implications for future treatment paradigms.

- Bone-Targeted Therapies in mCRPC:
    - Combination of enzalutamide and radium-223 is emerging as a potential first-line option in bone-dominant metastatic castration-resistant prostate cancer (mCRPC).
    - Skeletal-related events (SREs) remain a concern, emphasizing the need for bone-protective agents in these patients.
    - Bone-protective agents should also be considered for patients receiving AR pathway inhibitors (ARPIs) alone in mCRPC.

- Ongoing Trials & Future Directions:
    - ENZARAD trial will clarify the role of enzalutamide in high-risk localized prostate cancer.
    - Early data from STAMPEDE (adding abiraterone to RT + ADT for M0 disease) provide insights into how systemic intensification strategies may evolve.

- The future of treatment personalization may involve further stratification of patients based on disease biology and risk level.

Discussion Highlights:

- Ultra-Hypofractionation Considerations:
  - While SBRT is effective in intermediate-risk patients, longer follow-up is needed to assess potential late-onset toxicities.
  - Active surveillance remains the preferred strategy for most low-risk patients.

- Expanding the Role of Local RT in mHSPC:
  - Combination approaches (RT + systemic therapy) are proving beneficial in low-volume disease, but further data are needed for high-volume cases.

- Managing Bone Health in mCRPC:
  - Proactive use of bone-protective agents should be emphasized to reduce fracture risk and skeletal complications.

Conclusion:

Dr. Gillessen's presentation highlighted key advances in radiation therapy, systemic intensification, and bone-targeted strategies in prostate cancer. The field is shifting toward more personalized, multimodal treatment approaches, with ongoing trials shaping future practice in both localized and metastatic settings.

Bladder Cancer - Prof. Petros Grivas

Unfortunately, Prof. Grivas did not participate in the live chat. However, we released a post that wraps up his presentation:

https://x.com/OncoAlert/status/1886469723820376096

GU Radiotherapy - Dr. Sean Mcbride

Key Takeaways:

- RADICALS-HD Trial: ADT Duration & Postoperative Radiotherapy
  - Evaluated the role of androgen deprivation therapy (ADT) duration in patients receiving postoperative radiotherapy after radical prostatectomy.
  - No significant survival benefit was observed with long-term ADT compared to short-term or no ADT.
  - Highlights the importance of patient selection to balance treatment benefits vs. unnecessary ADT exposure.
  - Renal function impact:
    1. Decline in eGFR over time suggests a need for nephroprotective strategies and structured follow-up, particularly in patients with borderline kidney function.

2. Emphasizes proactive monitoring to optimize long-term treatment safety.

- NRG-GU003 Trial: HYPORT vs. COPORT in Post-Prostatectomy Radiotherapy
    - Compared hypofractionated post-prostatectomy radiotherapy (HYPORT) vs. conventional post-prostatectomy radiotherapy (COPORT).
    - HYPORT led to greater short-term GI toxicity but symptoms resolved within 6 months.
    - No significant long-term differences in genitourinary or GI toxicity.
    - Established HYPORT as a noninferior and acceptable new practice standard.

Discussion Highlights:

- Optimizing ADT Use in Post-Prostatectomy Radiotherapy:
    - Patient stratification remains critical in determining who benefits most from short-term vs. long-term ADT.
    - The absence of a clear survival advantage with prolonged ADT suggests a shift toward individualized treatment approaches.

- Balancing Efficacy & Toxicity in Radiotherapy:
    - HYPORT's noninferiority supports its integration into clinical practice.
    - While short-term GI toxicity is a concern, the lack of long-term differences in outcomes reinforces its viability as a standard option.

Conclusion:

Dr. Morgan's discussion of GU radiotherapy updates provided important insights into treatment personalization in prostate cancer. The RADICALS-HD trial informs decisions on ADT duration, while NRG-GU003 supports HYPORT as a new radiotherapy standard. Careful patient selection and toxicity management remain central themes in optimizing outcomes.

Urology In 2024 - Dr. Declan Murphy and Dr. Renu Eapen

Key Takeaways:

- The Impact of GU Cast on Medical Education & Professional Development
    - Podcasts like GU Cast have transformed medical education by offering accessible, real-time expert discussions beyond traditional formats.
    - They provide a platform for different voices in urology and GU oncology, fostering both agreement and debate, which is essential in scientific discourse.

- Podcasts vs. Traditional Scientific Journals
    - Podcasts offer a faster, more engaging, and simplified way to disseminate medical knowledge compared to traditional journals.

- Allow for diverse perspectives on key trials, making them an effective complement to peer-reviewed literature.
- Examples of other impactful medical podcasts:
    1. Uromigos – another respected urology-focused podcast.
    2. OncoAlert Newsletter's upcoming podcast expansion – reflects the growing importance of this medium in medical education.

- Social Media's Role in Expanding Medical Education
    - GU Cast actively leverages social media to extend its reach and engage with a global audience.
    - Platforms like Twitter (X), LinkedIn, and YouTube help amplify key discussions and connect professionals in real time.
    - Similar approaches are used by OncoAlert and Uromigos to disseminate key updates efficiently.

Practice-Changing Urology Trials in 2024:

1. Standard vs. Extended Lymphadenectomy for Muscle-Invasive Bladder Cancer
    - Findings: No survival benefit from extended lymphadenectomy into the peritoneum, with some patients experiencing harm.
    - Impact: Reinforces the need for patient selection and cautious surgical approaches.

2. Pelvic Lymph Node Dissection in Prostate Cancer
    - Findings: Update from a randomized trial comparing limited vs. extended dissection.
    - Impact: Provides critical guidance on lymph node dissection strategies in prostate cancer management.

3. Adjuvant Pembrolizumab in Renal-Cell Carcinoma
    - Findings: Overall survival benefit with adjuvant pembrolizumab in renal cell carcinoma.
    - Impact: Strengthens the role of immune checkpoint inhibitors in the adjuvant setting.

Conclusion:

Drs. Murphy and Eapen provided an insightful overview of major urology trials in 2024, emphasizing the evolving role of podcasts in medical education and knowledge dissemination. GU Cast's ability to engage a broad audience, foster discussion, and provide expert insights makes it a valuable complement to traditional journals. The highlighted urology trials reinforce shifts in surgical and systemic treatment strategies, guiding future practice.

Trials That Have Changed the Landscape in 2024 in GU Oncology - Dr. Maria Jose Juan Fita and Dr. Elena Sevillano

Key Takeaways:

Dr. María José Juan Fita

- ARANOTE Trial:
    - Findings: Another doublet therapy showing improved radiographic progression-free survival (rPFS), but without mature overall survival (OS) data.
    - Impact: Reinforces the importance of early intensification strategies in metastatic hormone-sensitive prostate cancer (mHSPC), but OS data will be key for widespread adoption.

- PSMAFORE Trial:
    - Ethical Concerns: Some debate regarding the control arm selection, raising questions about trial design and equipoise in modern clinical trials.

- RETAIN Trial:
    - Findings: A biomarker-driven approach to personalize treatment.
    - Impact: Highlights the growing role of precision medicine in GU oncology.

- NIAGARA Trial:
    - Findings: Positive for PFS and OS, but the necessity of adjuvant immunotherapy (IO) for all patients remains questionable.
    - Key Consideration: Patients achieving pT0 (complete pathological response) may not require adjuvant IO, underscoring the need for better patient stratification.

- AMBASSADOR Trial:
    - Findings: Primary endpoint met, but OS benefit remains unclear—awaiting final results.

- Pembro-EV in Metastatic Urothelial Carcinoma (mUC):
    - Impact: Set to become a first-line standard of care, with increased familiarity in managing immune-related toxicities.

- Lutetium-Based Therapies:
    - Findings: Demonstrates a clear rPFS advantage.
    - Impact: Could be prioritized earlier in treatment sequencing, though patient selection remains a critical factor.

- JAVELIN vs. EV302:

- Challenge: Selecting patients for these trials remains complex, as median OS differs (25.9 months vs. 31.5 months), requiring further refinement of treatment selection criteria.

Dr. Elena Sevillano

- KEYNOTE-564 Trial (Adjuvant Pembrolizumab in RCC):
  - Findings: Demonstrated a disease-free survival (DFS) benefit.
  - Consideration: Translating DFS gains into OS benefit remains challenging, but long-lasting immune responses suggest some patients may derive sustained benefits.

- IMmotion 010 Trial & KIM-1 Biomarker:
  - Findings: Trial did not meet its primary endpoint, but KIM-1 emerged as a promising biomarker.
  - Impact: KIM-1 could play a key role in future adjuvant strategies, serving as both a prognostic and potentially predictive biomarker.

- The Role of GUARD Consortium in GU Oncology:
  - Mission: Establishes an integrative platform for clinical and translational research.
  - Multidisciplinary Approach: Involves experts from medical oncology, urology, radiation oncology, pathology, molecular biology, radiology, and oncological pharmacy.
  - Global Reach: Collaborates both nationally and internationally to enhance diagnosis and treatment strategies.

Discussion & Future Directions:

- Discontinuation of IO + TKI in Metastatic RCC:
  - Key Question: When to stop treatment in patients with a good response to IO + TKI combinations?
  - Considerations: Identifying the optimal point to de-escalate therapy safely without compromising long-term outcomes.

Conclusion:

Drs. Juan Fita and Sevillano provided an in-depth review of pivotal trials shaping GU oncology in 2024, highlighting new treatment strategies, biomarker-driven approaches, and evolving roles of immunotherapy and radioligand therapy. The GUARD Consortium's contribution to translational research and multidisciplinary collaboration underscores its importance in advancing patient care worldwide.

The Patient Advocate Perspective - Mr. Bryan Lewis

Key Takeaways:

- KidneyCAN's Mission & Impact:

  Focuses on accelerating cures for kidney cancer by:

  1- Advocating for increased government and industry funding.

  2- Fostering collaboration between researchers and clinicians.

  3- Providing direct financial support to innovative kidney cancer research.

  4- Empowering patients and caregivers through educational outreach and access to clinical trials.

- Major Contributions to Kidney Cancer Research:
  - $50 million allocated in 2023 specifically for kidney cancer research.
  - Total of $285 million raised for research initiatives to date.
  - Grassroots advocacy efforts have played a crucial role in securing these funds.

- The Importance of Patient Advocacy
  - Groups like KidneyCAN are instrumental in shaping the research landscape.
  - Beyond funding, they connect patients with clinical trials, helping to expand access to cutting-edge treatments.
  - Their work highlights the power of community-driven initiatives in advancing cancer care.

Conclusion:

Mr. Bryan Lewis provided a compelling look into the patient advocacy perspective, emphasizing the critical role of funding, collaboration, and patient empowerment in the fight against kidney cancer. KidneyCAN's achievements underscore the importance of grassroots movements in driving meaningful progress in cancer research.