

## Best of ASTRO Patient Takeaways

Across the world, radiation oncologists are actively researching safe and effective radiation treatments, including more personalized approaches and studies of lower doses for a variety of cancers. The following research studies were presented during the ASTRO Annual Meeting in October 2020. Annually, ASTRO hosts the largest gathering of radiation oncology professionals in the world to share the latest science and research, all designed to improve patient care, support clinical practice and advance science and research in the field of radiation oncology.

The information provided below highlights the research provided in the studies included in the Best of ASTRO onDemand course. This information is not intended as medical advice. It is important to review and discuss all treatment options, including radiation therapy with your primary care physician before determining which option or combination of options is best for you and your lifestyle.

### Breast

**Discussant: Rachel Blitzblau, MD, PhD**

**Patient Takeaways prepared by Rachel Blitzblau, MD, PhD, and Jolinta Lin, MD**

#### **Several studies looked at alternative fractionation schemes for breast cancer radiation therapy (RT):**

- For early-stage breast cancers:
  - Accelerated partial breast RT to the tumor bed using twice daily fractions of 4 Gy in 8 treatments to 32 Gy showed effective treatment, lower rates of toxicities and better cosmetic outcome at 10 years of follow-up compared to higher doses per fraction (#25: Tagian et al.)
  - Alternative fractionations using simultaneous integrated lumpectomy cavity boost during whole breast RT in the IMRT-MCE2 and HYPOSIB trials demonstrated comparable local control outcomes and cosmesis compared to conventionally fractionated whole breast RT with boost (#19: Hörner-Rieber et al. & 24: Krug et al.)
- For HER2+ breast cancers:
  - An analysis of the HERA trial showed that HER2-positive patients who completed locoregional therapy, chemotherapy and HER2-directed therapy had excellent rates of local control regardless of whether or not a lumpectomy cavity boost was delivered; however, the authors advise that this decision should be studied in future randomized studies (#52, Zeidan et al.).
- For patients requiring post-mastectomy RT in the setting of reconstruction surgery:
  - A phase II trial consisting of hypofractionated chest wall and regional nodal irradiation is safe and effective with similar outcomes of reconstruction failures compared to those reported in literature from conventionally fractionated post-mastectomy RT (#20: Yehia et al.).

#### **Two studies focused on treatment toxicities:**

- Green tea extract, epigallocatechin-3-gallate (EGCG), may be effective in decreasing high grade skin irritation during post mastectomy RT compared to patients who received placebo (#22: Zhu et al).
- A prediction model calculating acute coronary events after breast RT showed the large impact of pre-existing comorbid conditions in increasing the risk of cardiac events (#21: Spoor et al.).

**For patients who convert from node positive disease to node negative disease after neoadjuvant chemotherapy:**

- A pooled analysis of four large prospective trials suggests that patients with residual disease in the breast had worse survival and higher rates of disease recurrence compared to those who had no residual disease in the breast; the authors caution against omitting regional nodal RT off clinical trial in this setting (#49: Mailhot et al).

## **CNS**

**Discussant: Jona Hattangadi-Gluth, MD**

**Patient Takeaways prepared by Jona Hattangadi-Gluth, MD, and Shiram Kharod, MD**

- Radiotherapy approaches for primary and metastatic brain tumor patients are evolving, with a focus on sparing of normal structures.
  - However, higher doses of IMRT radiotherapy does not improve overall survival in patients with glioblastoma when compared with standard doses.
- Glioblastomas are very aggressive and often incurable brain tumors, despite treatment with surgery, radiation and chemotherapy.
  - A new phase II trial was created to see whether adding Metformin, a commonly prescribed medicine used for diabetes, to existing treatments can improve cure rates for glioblastoma.
  - In this study, adding Metformin was found to be associated with improved treatment outcomes, though the sample size was small, and more data will be needed before making this a standard practice.
- When cancer spreads to the brain, there are different forms of radiation that is prescribed, depending on the size, number and location of the new cancerous spots.
  - We've just learned from a new phase III randomized controlled trial that we can use stereotactic radiosurgery, a very precise and focused type of radiation treatment, to treat patients who have four to 15 separate spots of cancer in their brain.
  - This is important, because in the past, radiation to the entire brain would have to be prescribed for these patients. By being able to treat these patients with more precise forms of radiation, they will likely experience fewer side effects, such as changes in cognitive function, than before.
  - Novel trials and novel imaging may allow better targeting of tumors and better preservation of neurocognitive function among patients with brain tumors.

## **Gastrointestinal**

**Discussant: Daniel Chang, MD**

**Patient Takeaways prepared by Daniel Chang, MD**

- Patients with rectal cancer may be able to successfully be managed with close surveillance and avoid surgery, but further study is needed to better understand which patients for whom this strategy is safest.

- Genetic signatures in the tumor may be able to help predict which patients can be managed with observation.
- Detectable fragments of tumor DNA circulating in the bloodstream could serve as early markers of response to treatment for esophageal cancer after curative chemotherapy and radiation.
- For patients who receive radiation for pancreatic cancer, the dose to the nearby blood vessels may be important for disease control given the risk of tumor spread.
- Stereotactic body radiotherapy (SBRT) for hepatocellular carcinoma is a highly effective treatment with excellent local control.
- Combining SBRT with immune therapy could improve the efficacy of treatment.

## Genitourinary

**Discussant: Gerard Morton, MD**

**Patient Takeaways prepared by Michael Corradetti, MD, PhD**

- Prostate cancer patients with intermediate- and high-risk disease may benefit from a higher, boosted dose of radiation therapy (RT).
  - Multiple trials have shown promise investigating a variety of boost techniques:
    - The ASCENDE RT trial employed a brachytherapy (“internal” RT) boost.
    - The HYPOPROST trial employed an ultrahypofractionated (i.e., a higher dose per treatment) boost.
    - The FLAME trial demonstrated that a focal lesion within the prostate could be identified by MRI and “microboosted” to a high dose.
- Short-term androgen deprivation therapy (ADT) works synergistically with RT in prostate cancer patients to enhance its efficacy and may reduce the toxicity of treatment by reducing the size of the prostate.
  - It remains controversial whether patients benefit from a period of ADT prior to the initiation of RT, or whether ADT can start concurrently with RT.
  - The HERO trial demonstrated that Relugolix is a promising oral ADT option which may become preferable to injectable options, especially in patients with pre-existing heart disease.
- Patients with locally recurrent prostate cancer after RT may benefit from salvage brachytherapy.
  - Local recurrence or persistence of disease occurs in 10-30% of patients following definitive RT. In many instances, these patients are managed with palliative intent.
  - The NRG/RTOG 0526 trial demonstrated that brachytherapy is a promising alternative curative option which compares favorably to salvage prostatectomy.
- Accurate imaging is essential to guide treatment in patients with recurrent prostate cancer after prostatectomy.
  - The EMPIRE-1 trial utilized Fluciclovine PET/CT to better define patients who are more likely to benefit from salvage RT and helped the radiation oncologist delineate the radiation plan. There were improved outcomes in patients who received this type of “molecular imaging.”
- The optimal treatment of bladder cancer patients who undergo bladder conservation therapy (i.e., nonsurgical treatment) has yet to be defined.

- The NRG/RTOG 0712 trial compared two chemoradiation regimens and demonstrated that daily RT plus gemcitabine is a suitable option versus cisplatin in the definitive treatment of locally advanced bladder cancer patients.
- Patients with kidney cancer with oligoprogressive disease (i.e., cancer that progresses at only one or a few sites) may benefit from focal treatment with stereotactic body radiation therapy (SBRT).

## Gynecologic

**Discussant: Jyoti Mayadev, MD**

**Patient Takeaways prepared by Jyoti Mayadev, MD**

- Our understanding of the genomics of cervical cancer and the tumor microenvironment is rapidly evolving.
- Major advances in clinical outcomes for locally advanced cervical cancer are on the horizon via immunotherapy.
- Safely reducing our treatment volumes in cervical cancer radiation with intensity-modulated radiation therapy (IMRT) can only lead to improved quality of life as our patients live longer.

## Hematologic

**Discussant: John Plastraras, MD, PhD**

**Patient Takeaways prepared by John Plastraras, MD, PhD**

**Ntentas et al: An excess mortality risk analysis of proton beam versus optimal photon radiotherapy for Mediastinal Hodgkin lymphoma: Who may benefit the most?**

- Which patients with lymphoma may benefit most from proton radiation therapy? If the lymphoma overlaps significantly with the heart, it is predicted that fewer of these patients will have heart complications decades later if proton therapy is used.

**Shelley et al: Efficacy of low dose radiotherapy in head and neck MALT lymphoma**

- What is the best radiation dose for patients with low grade non-Hodgkin lymphoma (MALT lymphoma) in the head and neck? Moderate doses of radiation (24-25 Gy) can control tumors better than very low doses (4 Gy), but both moderate and very low doses may be appropriate depending on the situation, such as in patients with Sjögren syndrome, which can cause dry mouth on its own.

**Price et al: Effective pain control with very low dose palliative radiotherapy for multiple myeloma patients with painful osseous lesions**

- Very low doses (4-8 Gy) given in one to two treatments may be help with pain in patients with multiple myeloma, which is much lower than what has been used in the past.

**Manjunath et al: Is bridging radiation (RT) safe with B cell maturation antigen-targeting chimeric antigenic receptor T cells (CART-BCMA) therapy? and**

## **Mikhaeel et al: Bridging radiotherapy before CAR-T for high grade lymphoma – Feasibility and Efficacy**

- “Bridging radiation” can be used for patients with either multiple myeloma or aggressive non-Hodgkin lymphoma who are undergoing CAR-T cell therapy safely and without interfering with these exciting new cellular therapies.

## **Lung/Thoracic**

**Discussant: Andreas Rimner, MD**

**Patient Takeaways prepared by Andreas Rimner, MD**

### **Hess et al: Immunomodulatory low dose whole-lung RT for COVID-19-related pneumonia**

- Low dose whole lung RT appears to reduce lung inflammation from Covid-19
- Reduced inflammatory markers
- Reduced radiographic ARDS picture
- May reduce intubation rate
- May reduce time to clinical recovery
- Comparison to drug interventions not available
- May be complementary to drug intervention
- Long-term risks unknown

### **Higgins et al: Patterns of disease progression on IMPower 133**

- Atezolizumab improves the time to developing brain metastases compared to chemotherapy alone in patients with ES-SCLC.
- Prophylactic cranial irradiation can reduce the development of new brain lesions by about 10% in patients with ES-SCLC.
- Further studies on PCI vs observation, the role of hippocampal-sparing PCI in preserving neurocognitive function, and SRS for brain metastases from ES-SCLC are under way.

### **Siva et al: TROG 13.01 SAFRON II single fraction vs 4 fraction SABR**

- Stereotactic body radiation therapy (SABR) may be delivered as a single dose or few doses.
- SABR is a great, noninvasive treatment modality that results in high efficacy and local control with generally a low risk of side effects.
- Understanding of side effects in combination with novel drugs is still evolving.

### **Louie et al: A phase III randomized trial of palliative radiation for advanced central lung tumors with intentional avoidance of the esophagus (PROACTIVE)**

- Cardiac/coronary artery sparing needs to be optimized in radiation treatment planning:
  - Reduce major adverse cardiac events (MACE).
  - Consider optimizing cardiac care with a cardiologist.
- Effective esophageal sparing is possible with advanced radiation techniques:
  - Reduce patient-reported esophageal symptoms.

- Improve quality of life.
- Decrease objective esophagitis rates.

**Kong et al: RTOG0617 to externally validate blood cell ERCC1/2 genotypic signature as a radiosensitivity biomarker for both tumor and normal tissue for individualized dose prescription**

- Metformin plays no role in improving progression-free survival in stage III NSCLC treated with concurrent chemo-RT.
- Genotypic signatures of tumor and normal tissues will likely inform future individualized radiation treatment regimen.

## **Palliative Care**

**Discussant: Joshua Jones, MD**

**Patient Takeaways prepared by J. Ben Wilkinson, MD**

### **Influence of the Pain Duration on Pain Outcomes Following Palliative Radiotherapy**

Dr. Saito found that patients who have cancer-related pain for a shorter period of time before radiation therapy tend to have cancer-related pain for a shorter period of time after treatment. This research team also found that patients can live to develop other types of non-cancer pain as well.

### **Validation of Model for Estimating Life Expectancy with Bone Metastases**

A web-based software program called Oncospace looks like it can predict how long someone will live with cancer that has spread to the bone. In this abstract, researchers describe how community practice information was used to verify that this model is accurate.

### **Classifying Patients at Risk of Death at Time of Palliative Radiation Consult**

Several factors were shown to be linked with the chance of a patient dying quickly after palliative radiation. Some of these include age of the patient, performance status, whether there was cancer in the liver, the number of cancer metastasis, the albumin level in the blood and whether a patient had been in the hospital in the past three months.

### **Randomized Study Looking at Two Treatments of Ultra-Precise Radiation or Five Treatments of Lower Dose Radiation to the Spine**

Patients in both study groups had significant lowering of their pain. Two times more patients who received the higher-dose form of treatment (stereotactic) had a complete response of their pain compared to those who received the lower standard dose of radiation at both three months and six months.

### **Stereotactic Radiation Therapy for Non-Spine Bone Metastases**

Interesting information was included in this abstract that suggests high-dose, ultra-precise radiation therapy (stereotactic) treatment may have a higher degree of pain control in areas of cancer that have

spread to bones outside the spine. Data about using these types of high-dose treatments in areas other than the spine will be important in years to come.

### **Use of Targeted Therapy and Stereotactic Radiation Therapy for Large Tumors**

This abstract showed that mixing high-dose radiation therapy with a type of immune therapy (pembrolizumab) showed impressive rates of control of the tumor, even in patients where their whole tumor could not be fully covered by the radiation therapy because of its large size.

### **Long-Term Results of SABR-COMET Trial**

An update to a very important clinical trial was presented this year at ASTRO. In 2018, the SABR-COMET trial showed that treatment of limited areas of cancer spread (called oligometastatic disease) with ultra-precise, high-dose radiation therapy can lead to improved disease control and longer survival. In this update, both disease control and overall survival were still nearly two times higher when stereotactic treatment of limited sites of disease was included as part of the initial treatment plan.

### **Impact of Serious Illness Conversation on Length of Palliative Radiotherapy**

Researchers showed that having conversations on how serious a patient's illness is can influence the number of radiation treatments and total dose prescribed. The authors of this abstract also showed that more serious illness conversations were documented by medical oncologists than by radiation oncologists.

## **Patient Safety**

**Discussant: Eric Ford, PhD**

**Patient Takeaways prepared by Christian Okoye, MD**

Preventable errors are present throughout medicine and several investigators are using novel methods to identify and improve these gaps in care.

### **Miller et al: A Pilot Trial Using Telehealth in Radiation Oncology: The Future of Healthcare is Virtual**

- Prior to the COVID-19 pandemic, telehealth has not had an established role in radiation oncology.
- Visits to hospitals, including emergency departments and cancer centers, decreased at the start of the pandemic, and in many areas have not returned to 2019 levels.
- Telehealth in radiation oncology has the potential to improve health care access, address social determinants of health and improve patient outcomes.
- Patients with telehealth visits as their first visit after completing radiotherapy enjoyed high overall satisfaction, good communication and high levels of trust.
- Providers were able to properly assess symptoms and patient toxicity, without needing to bring patients in for an in-person evaluation.
- In conclusion, telehealth was well received by patients and providers and provided high enough quality for safe and effective post radiation care.

### **Prasad et al: Cardiovascular Event Reporting in Clinical Trials Involving Chest Radiation Therapy**

- Cardiovascular endpoints are major considerations for radiotherapy clinical trials.

- In a review of over 100 trials, over half reported no major adverse cardiac events and over one third reported no cardiovascular disease events.
- When compared to patients without cancer, the expected number of cardiovascular events during these trials is much higher than reported, suggesting these events are vastly underreported.
- Clinical trial designs should be improved to better identify cardiovascular events.

**Mazur et al: Effect of Neurofeedback and Simulation-based Training Interventions on Radiation Therapists' (RTTs) Mental Workload, Situation Awareness and Performance**

- Radiation therapists are often the last person available to identify an error before it gets propagated to the patient, therefore their ability to identify errors is critical.
- The addition of neurofeedback training to simulation-based training interventions significantly improves the error detection rate with minimal costs.
- Neurofeedback may improve the awareness of radiation therapists leading to a higher error detection rate.
- While unblended, the study showed encouraging results for simple, manageable and inexpensive and hold promise for wider adoption.

**Shumway et al: Machine Learning to Improve the Prioritization and Effectiveness of Pre-Treatment Physics Chart Checks**

- While quality check prior to treatment have been shown to be one of the most effective methods of catching errors, some charts have added complexity and require more attention to catch potential errors.
- Several attributes of patient charts that contribute to their difficulty, including clinical features, plan details, and quality assurance specifics, were reviewed and compared against the overall difficulty as assessed by physicists.
- The outcomes from computer algorithms correlated well with ratings assessed by physicists.
- The use of this screening tool can improve plan prioritization and allow physicist more time to review the more complex plans.
- These types of tools can be combined with the recently published AAPM Task Group 275, which has outlined strategies for effective plan and chart reviews.

**Zhang et al: Categorizing Incident Learning Reports by Narrative Text Clustering to Improve Safety**

- Incident learning systems (ILS) have been established to record incidents that happen within radiation clinics to inform future best practices.
- Current incident reports consist almost exclusively of text reports that require manual extraction of data to combine the data and make generalizations across separate experiences; this limitation makes the analysis of data impossible to accomplish on a large scale.
- A classification algorithm was used in an attempt to classify reports into 30 separate groups based on linguistic processing.
- The two markers that were used included term frequency (the number of times a specific word/term appears in a report) and inverse document frequency (the inverse of the number of times a word is present in a document).
- Clustering was able to identify several types of reports, including those related to external contours during radiation planning and patient face photos.
- This method is very attractive as it does not require any learning to separate cases.

- If it can be successfully expanded to independent datasets, it may be very helpful in processing larger, multi-institutional datasets.