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Critical Review

American Society of Clinical Oncology 2022 Annual Meeting Highlights for Radiation Oncologists

Austin P.H. Dove, MD,[a] Jeffrey Ryckman, MD,[b] Arpit Chhabra, MD,[c] Jason Beckta, MD, PhD,[d] and Mudit Chowdhary, MD[e,*]

[a]Department of Radiation Oncology, Vanderbilt University Medical Center, Nashville, Tennessee; [b]Department of Radiation Oncology, West Virginia University Medicine Camden Clark Medical Center, Parkersburg, West Virginia; [c]New York Proton Center, New York, New York; [d]Department of Radiation Oncology, University of Vermont Medical Center, Burlington, Vermont; and [e]Northside Radiation Oncology Consultants, Northside Hospital Cancer Institute, Atlanta, Georgia

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Abstract

The American Society of Clinical Oncology annual meeting is the largest multidisciplinary oncology-focused conference in the world. With almost 5000 total abstracts in 2022, it is difficult for individuals to evaluate all the results. Here we present a review of 28 selected abstracts, across all disease sites, focusing on those of greatest relevance to radiation oncologists.

Introduction

The American Society of Clinical Oncology annual meeting is the largest multidisciplinary oncology conference in the world. With the volume of research presented, evaluation of data presented can be challenging.[1] In our review, we present abstracts that were felt to be most pertinent to practicing radiation oncologists. Here, we succinctly present these 28 studies (Table 1), organized alphabetically by disease sites, for your convenience.

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*Corresponding author: Mudit Chowdhary, MD; E-mail: mchowdharymd@gmail.com

Breast

NRG-BR002: A phase IIR/III trial of standard of care systemic therapy with or without stereotactic body radiotherapy (SBRT) and/or surgical resection (SR) for newly oligometastatic breast cancer (NCT02364557)[2]

Studies of metastases-directed therapy (MDT) have shown significant improvements in progression-free survival (PFS) and overall survival (OS) in selected oligometastatic patients; however, there is limited prospective randomized evidence specifically in oligometastatic breast cancer.[3,4] NRG-BR002 was a phase 2R-3 randomized controlled trial (RCT) of patients with oligometastatic breast cancer (≤4 extracranial sites) who had controlled primary disease on first line therapy for ≤12 months who were

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Table 1 Selected presentations of interest involving radiotherapy from the American Society of Clinical Oncology 2022 annual meeting

Topic	Trial/study name	First author	Session type	Abstract number
Breast	NRG-BR002: A phase IIR/III trial of standard of care systemic therapy with or without stereotactic body radiotherapy (SBRT) and/or surgical resection (SR) for newly oligometastatic breast cancer (NCT02364557). Abstract	Chmura[2]	Oral	1007
Breast	LUMINA: A prospective trial omitting radiotherapy (RT) following breast conserving surgery (BCS) in T_1N_0 luminal A breast cancer (BC). Abstract 363918	Whelan[5]	Oral	LBA501
CNS	Phase II randomized study comparing proton craniospinal irradiation with photon involved-field radiotherapy for patients with solid tumor leptomeningeal metastasis	Yang[10]	Oral	2000
CNS	A controlled comparison of cerebral volume loss after brain irradiation with proton versus photon radiotherapy. Abstract 376740	Gardner[12]	Poster discussion	2017
GI	Single agent PD-1 blockade as curative-intent treatment in mismatch repair deficient locally advanced rectal cancer. Abstract LBA5	Cercek[13]	Oral	LBA5
GI	Contact x-ray brachytherapy (Papillon) in addition to chemoradiotherapy to improve organ preservation in early cT2-T3 rectal adenocarcinoma: The 3-year results of OPERA randomized trial (NCT02505750). Abstract 3512	Gerard[14]	Poster discussion	3512
GI	STAR-TREC phase II: Can we save the rectum by watchful waiting or transanal surgery following (chemo)radiotherapy versus total mesorectal excision for early rectal cancer? Abstract 3502	Bach[15]	Oral	3502
GI	Curative chemoradiation for low rectal cancer: Primary clinical outcomes from a multicenter phase II trial. Abstract LBA3514	Jensen[16]	Poster discussion	LBA3514
GI	Clinical and radiological predictors of organ preservation in patients with rectal cancer treated with total neoadjuvant therapy. Abstract 3619	Yuval[18]	Poster session	3619
GI	Randomized phase III trial of induction chemotherapy followed by chemoradiotherapy or chemotherapy alone for nonresectable locally advanced pancreatic cancer: First results of the CONKO-007 trial. Abstract 4008	Fietkau[19]	Oral	4008
GI	Randomized clinical trial on resection of the primary tumor versus no resection prior to systemic therapy in patients with colon cancer and synchronous unresectable metastases. Abstract LBA3507	Rahbari[20]	Oral	LBA3507
GU	Prostate-specific membrane antigen PET response associates with radiographic progression-free survival following stereotactic ablative radiation therapy in oligometastatic castration-sensitive prostate cancer. Abstract 375452	Sutera[23]	Poster discussion	5011
GU	Phase II, double-blind, randomized study of salvage radiation therapy (SRT) plus enzalutamide or placebo for high-risk PSA-recurrent prostate cancer after radical prostatectomy: The SALV-ENZA trial. Abstract 369496	Tran[24]	Poster discussion	5012
GU	Impact of PSMA PET/CT on prostate cancer salvage radiotherapy management: Results from the prospective randomized phase 3 trial [PSMA SRT NCT03582774]. Abstract 5028	Armstrong[25]	Poster session	5028
H&N	Radiotherapy alone versus concurrent chemoradiotherapy in intermediate risk nasopharyngeal carcinoma: A multicentre, open-label, noninferiority, randomised phase III trial. Abstract 375158	Ma[26]	Oral	6000
H&N	Nimotuzumab plus chemoradiotherapy versus placebo plus chemoradiotherapy in patients with locally advanced nasopharyngeal carcinoma (NPC): A prospective, randomized-controlled, double-blinded, multicenter phase III clinical trial. Abstract 380336	Sun[27]	Oral	6001

(*continued on next page*)

Table 1 (*Continued*)

Topic	Trial/study name	First author	Session type	Abstract number
H&N	Reduced-dose radiotherapy for pretreatment EBV DNA selected low-risk stage III nasopharyngeal carcinoma: A single-arm, phase II trial. Abstract 363298	Mai[28]	Oral	6002
H&N	An open-label, noninferiority phase III RCT of weekly versus three weekly cisplatin and radical radiotherapy in locally advanced head and neck squamous cell carcinoma (ConCERT trial). Abstract 377958	Sharma[29]	Oral	6004
H&N	Results of phase 3 randomized trial for use of docetaxel as a radiosensitizer in patients with head and neck cancer unsuitable for cisplatin-based chemoradiation. Abstract LBA6003	Patil[31]	Oral	LBA6003
H&N	ROMAN: Phase 3 trial of avasopasem manganese (GC4419) for severe oral mucositis (SOM) in patients receiving chemoradiotherapy (CRT) for locally advanced, nonmetastatic head and neck cancer (LAHNC). Abstract 369072	Anderson[32]	Oral	6005
H&N	Effectiveness of adjuvant chemoradiotherapy for oral cavity squamous cell carcinoma with minor and major extranodal extension: A multi-institutional consortium study. Abstract 364062	Manojlovic Kolarski[33]	Poster discussion	6010
Heme	First-line brentuximab vedotin plus chemotherapy to improve overall survival in patients with stage III/IV classical Hodgkin lymphoma: An updated analysis of ECHELON-1. Abstract 7503	Ansell[34]	Oral	7503
PED	Brentuximab vedotin and association with event-free survival (EFS) in children with newly diagnosed high-risk Hodgkin lymphoma (HL): A report from the Children's Oncology Group phase 3 study AHOD1331 (NCT 02166463). Abstract 7504	Castellino[35]	Oral	7504
Thoracic	Comparison of quality of life in patients randomized to high-dose once daily (QD) thoracic radiotherapy (TRT) with standard twice daily (bid) TRT in limited stage small cell lung cancer (LS-SCLC) on CALGB 30610 (Alliance, Sub-study CALGB 70702). Abstract 376466	Ganti[37]	Oral	8504
Thoracic	Improved survival from early combined radiotherapy: A phase II clinical study and underlying mechanisms of delaying EGFR-TKI acquired resistance in patients with advanced lung cancer	Zhang[38]	Poster	9114
Thoracic	Two-year update from KEYNOTE-799: Pembrolizumab plus concurrent chemoradiation therapy (cCRT) for unresectable, locally advanced, stage III NSCLC. Abstract 375944	Reck[40]	Poster discussion	11550
Thoracic	Consolidation nivolumab plus ipilimumab or nivolumab alone following concurrent chemoradiation for patients with unresectable stage III non-small cell lung cancer: BTCRC LUN 16-081. Abstract 378288	Durm[41]	Poster discussion	8509
Sarcoma	Outcomes following preoperative chemoradiation +/- pazopanib in non-rhabdomyosarcoma soft tissue sarcoma (NRSTS): A report from Children's Oncology Group (COG) and NRG Oncology. Abstract 375912	Weiss[42]	Oral	11504

Abbreviations: CNS = central nervous system; CT = computed tomography; EBV = Epstein-Barr virus; EGFR = epidermal growth factor receptor; GI = gastrointestinal; GU = genitourinary; H&N = head and neck; NSCLC = non-small cell lung cancer; PET = positron emission tomography; RCT = randomized controlled trial; TKI = tyrosine kinase inhibitors.PD-1 = Programmed cell death protein 1; PSA = Prostate-Specific Antigen; PSMA = Prostate-Specific Membrane Antigen; PED = Pediatrics.

randomized to standard-of-care systemic therapy alone ± MDT to all metastases. A total of 125 of 129 patients were eligible. Most patients in the MDT arm received SBRT (93%). Of note, 5% in the MDT did not receive ablation. With a median follow-up (MFU) time of 30 months, the investigators showed no signal for improved PFS or OS between arms. No subgroup showed benefit to MDT, including those with single versus multiple metastasis or circulating tumor cell counts (0 vs ≥1). As such, the trial will not proceed to the phase 3 component. The results of this study highlight the heterogeneity of oligometastatic disease across different cancer histologies. Further study is needed to find the subset of patients with metastatic breast cancer who may benefit from MDT.

LUMINA: A prospective trial omitting radiotherapy (RT) following breast conserving surgery (BCS) in T_1N_0 luminal A breast cancer (BC)[5]

In this prospective multicenter cohort study, the investigators assessed the impact of forgoing adjuvant RT following BCS (≥1-mm surgical margin) in select patients with breast cancer receiving adjuvant hormone therapy. Eligibility criteria included women ≥55 with grade 1 to 2 T1N0 breast cancer, luminal A subtype (ER ≥1%, PR ≥20%, HER-2 negative, Ki67 ≤13.25%). The primary outcome was to show the upper bound confidence interval (CI) for LR to be <5% for any invasive or noninvasive cancer in the ipsilateral breast; 501 patients were enrolled. The median age was 67 and median tumor size was 1.1 cm. With an MFU of 5 years, the LR rate was 2.3%. Five-year contralateral breast cancer, relapse free-survival, disease-free survival (DFS), and OS were all favorable as well. The authors suggest that these patients are candidates for RT omission. We suggest caution with this interpretation, however, given the nonrandomized single-arm study design, short follow-up, multiple studies showing continued LR rates beyond 5 years for favorable breast cancer, and advances in RT improving both convenience and cost while preserving efficacy.[6-9]

Central Nervous System

Phase II randomized study comparing proton craniospinal irradiation with photon involved-field radiotherapy for patients with solid tumor leptomeningeal metastasis[10,11]

In a single institution phase 2 study, 63 patients were randomized in a 2:1 ratio to proton craniospinal irradiation (pCSI) and photon involved-field RT (IFRT) for patients with leptomeningeal metastases with primary histology either non-small cell lung cancer (NSCLC) or breast cancer. Eligibility criteria included radiographic and/or cytology confirmed leptomeningeal metastases with Karnofsky Performance Scale (KPS) ≥60. Baseline factors including age, histology, and active systemic disease were controlled for. In addition, 35 patients with all other solid tumor histologies were enrolled in an exploratory pCSI. RT was 30 Gy/10 fractions (fx) for all patients with primary endpoint of central nervous system (CNS) PFS with secondary endpoints of OS and treatment-related adverse effects. At planned interim analysis, significant benefit in CNS PFS was seen with pCSI with a median PFS of 7.5 months compared with a median of 2.0 months with IFRT ($P \leq .001$). In addition, pCSI demonstrated improved median survival at 8.2 versus 4.9 months with IFRT ($P = .04$). Grade 3 nonheme Treatment Adverse Effects (TAE)s were seen in 3 patients in the pCSI arm and 5 patients in the IFRT arm. As a result, early discontinuation of trial was recommended. Of note, in the exploratory pCSI arm, 57% had active systemic disease, with ovarian cancer being the most common histology (20%). At MFU of 9.6 months, 20% of patients had CNS progression and 57% died. The median PFS was 5.4 months and OS was 6.6 months, with 4 patients having grade 3 treatment adverse events. This study confirms an improved CNS PFS and OS benefit for patients undergoing pCSI versus IFRT with similar grade 3 or higher toxicity. One criticism of the study would be the limitation of comparing outcomes with different field sizes of photon field versus proton CSI.

A controlled comparison of cerebral volume loss after brain irradiation with proton versus photon radiotherapy[12]

A retrospective case-matched control series of World Health Organization patients with grade 2 or 3 glioma evaluated change in ventricular volume in patients treated with proton and photon RT as a surrogate for neurotoxic effects of treatment. Patients were retrospectively selected and individually matched, with proton and photon patients using an 11-tiered criterion. Patients were only included if they had at least 2 years of PFS and available magnetic resonance imaging (MRI) at baseline, 1 year, and 2 years following RT. Cerebral volume loss was estimated using measurement of ventricular volume in the tumor-free hemisphere. When comparing 2-year MRI, change in ventricular volume of the photon group was 24.85% (standard deviation, 14.45%) and 12.03% (standard deviation, 16.3%) in the photon group. One-way analysis of variance showed that ventricular volume increase after 2 years was statistically greater in photon versus proton group ($F[1, 32.00], 5.90; P < .021$). While limited, this study suggests proton therapy could potentially reduce neurotoxicity within the tumor-free hemisphere. Ongoing studies such as NRG-BN005 comparing longitudinal cognitive outcomes between photon and proton treatment in patients with brain tumors could provide more evidence of functional neurologic outcomes between the 2 groups.

Gastrointestinal

Single agent PD-1 blockade as curative-intent treatment in mismatch repair deficient locally advanced rectal cancer[13]

Approximately 5% to 10% of patients with rectal cancer are mismatch-repair deficient (MMRd), and these tumors

have been shown to respond poorly to standard chemotherapy regimens. This phase 2 study investigated dostarlimab alone (anti- Programmed cell death protein 1(PD-1)) every 3 weeks up to 6 months for patients with MMRd stage II to III locally advanced rectal cancer. Patients who had complete response (CR) were to proceed without definitive local therapy. At an MFU of 12 months, all 12 patients had a CR with no evidence of tumor on MRI, positron emission tomography (PET)/computed tomography (CT), endoscopy, palpation, or biopsy. At the time of the report, no patients had received chemoradiation therapy (CRT) or undergone surgery, and no cases of progression or recurrence had been reported during follow-up at a range of 6 to 25 months. There were no grade 3 adverse events reported. The authors concluded MMRd locally advanced rectal cancer is highly sensitive to single agent PD-1 blockage, but longer follow-up is needed to assess the duration of response, as only 4 patients are responding more than 1 year after treatment.

Contact x-ray brachytherapy (Papillon) in addition to chemoradiotherapy to improve organ preservation in early cT2-T3 rectal adenocarcinoma: The 3-year results of OPERA randomized trial (NCT02505750)[14]

STAR-TREC phase II: Can we save the rectum by watchful waiting or transanal surgery following (chemo)radiotherapy versus total mesorectal excision for early rectal cancer?[15]

Curative chemoradiation for low rectal cancer: Primary clinical outcomes from a multicenter phase II trial[16]

Three trials (OPERA, STAR-TREC, WW2) investigated organ preservation (OP) after CR in rectal cancer in a similar, mostly ≤T3b (ie, ≤5-mm depth of invasion beyond the outer border of the muscularis propria) and mostly cN0 (71%-100%) population (Table E1). These studies of early-stage rectal cancer were designed to spare the use of consolidative or induction FOLFOX and encourage the potential role for microsurgery of local regrowth, and all 3 trials demonstrated a promising 1- to 3-year OP rate of at least 60% (Table E1). OPERA, a phase 3 trial, enrolled 144 patients with ≤5-cm diameter tumors and was stratified by tumors ±3 cm. After an initial 45 Gy/25 fx with concurrent capecitabine, patients were randomized to receive a boost with conventional RT (9 Gy/5 fx over 1 week) versus Papillon contact x-ray brachytherapy (CXB; 90 Gy/3 fx over 4 weeks).[17] The authors conclude an CXB boost, when combined with CRT, increases the OP rate in early rectal adenocarcinoma, especially for tumors <3 cm. STAR-TREC, a rolling phase 2/3 trial, enrolled 120 patients with ≤4-cm diameter tumors, and the phase 2 portion randomly allotted patients 1:1:1 to total mesorectal excision (TME) or short-course radiation (25 Gy/5 fx) versus long-course CRT (LC-CRT; 50 Gy/25 fx with concurrent capecitabine). The phase 3 portion will be a partially randomized patient preference study, where patients select either TME surgery or OP. As OP rates were >50% in the phase 2 study to inform trial design, the phase 3 partially randomized patient-preference study will continue as planned. WW2, a prospective observational phase 2 trial, enrolled 107 patients with tumors <6 cm from the verge. Patients were treated with 50.4 Gy/28 fx to the regional lymph nodes and 62 Gy/28 fx to gross disease with concurrent capecitabine. Clinical complete response (cCR) was nearly 90%, which compares favorably with the CXB cohort from OPERA. Together, these 3 trials suggest promising OP strategies, which may spare the use of FOLFOX and encourage the potential role for microsurgery of local regrowth for patients with initial cCR without an apparent detriment in distant recurrences for patients appropriately allocated to surveillance endoscopy and MRI every 3 months after the completion of RT.

Clinical and radiological predictors of organ preservation in patients with rectal cancer treated with total neoadjuvant therapy[18]

A posthoc analysis of OPRA investigated multivariable analysis of predictors for OP (Table E1). As a reminder, OPRA was a total neoadjuvant therapy study of more advanced rectal tumors (eg, 78% T3, 15% T4, and 71% N+) randomizing 324 patients with MRI-staged stage II to III rectal cancer amenable to TME treated with preoperative LC-CRT preceded (induction arm) or followed by (consolidative arm) FOLFOX/CAPEOX for 16 to 18 weeks. Three-year rates of OP were 41% in the induction chemotherapy arm and 53% in the consolidative chemotherapy arm, suggesting upfront LC-CRT followed by consolidative chemotherapy may be the preferred strategy for OP. However, there was no difference in 3-year DFS (76%) or distant metastasis-free survival (82%), suggesting either induction or consolidative chemotherapy approaches are valid for disease control. Independent predictors of OP on multivariate analysis (MVA) included node-positive disease (hazard ratio [HR], 1.89; 95% CI, 1.23-2.90), extramural venous invasion (HR, 1.63; 95% CI, 1.02-2.59), and involved circumferential resection margin (CRM; HR, 1.55; 95% CI, 1.05-2.28), while tumor length (HR, ∼1.1; 95% CI, 0.99-1.23) and upfront CRT (HR, ∼0.76; 95% CI, 0.54-1.07) were insignificant. Considering node-positive disease had the largest hazard ratio for independent prediction of OP on OPRA, induction or

consolidative chemotherapy may be preferred when pursuing OP strategies in patients with node-positive disease.

Randomized phase III trial of induction chemotherapy followed by chemoradiotherapy or chemotherapy alone for nonresectable locally advanced pancreatic cancer: First results of the CONKO-007 trial[19]

CONKO-007 is a phase 3 study investigating the role of induction chemotherapy (gemcitabine or FOLFIRINOX) followed by CRT (50.4 Gy/28 fx with gemcitabine) or the same chemotherapy agent in patients with nonresectable locally advanced pancreatic cancer. After 3 months of induction chemotherapy, 190 out of 525 patients were excluded because of progression or toxicity, leaving 335 patients to be randomized. If possible, surgery was allowed and a little over one-third of patients proceeded to surgery. At an MFU of 16 months, there was no difference in median PFS or OS in the CRT arm, but PFS tended to be higher in the CRT arm after 2 years (24% vs 18%). A positive CRM (<1 mm) appeared to influence 2-year OS in the context of a CRM-negative resection (41% vs 67%). CRT increased the rate of R0 CRM negative resections (20% vs 9%), decreased R1 resections (3% vs 10%), and increased pathologic complete response (pCR) (0% vs 6%) without difference in PFS or OS. Although there was no difference in OS, the 5-year OS was doubled (4% vs 10%) in patients receiving RT. Among the subgroup of patients undergoing surgery and receiving FOLFIRINOX, 5-year OS was 13% for preoperative chemotherapy alone and 27% for RT. RT may prolong the survival tail, similarly to PREOPANC. The role of dose-escalation and advanced RT technology in this setting will be key.

Randomized clinical trial on resection of the primary tumor versus no resection prior to systemic therapy in patients with colon cancer and synchronous unresectable metastases[20]

Pooled outcomes for 2 phase 3 trials investigating upfront primary tumor surgery for metastatic colon cancer with unresectable synchronous metastases and asymptomatic primary tumors were reported; 295 patients from SYNCRONOUS and 98 patients from CCRe-IV comprised the cohort, with an MFU of 37 months. OS was not improved with the addition of upfront primary tumor surgery (16.7 vs 18.6 months; $P = .685$). Failure to receive chemotherapy was more common (6% vs 24%), although serious adverse events (excluding postoperative complications) were decreased (20% vs 13%) with upfront primary tumor resection. Sixty-day mortality and postoperative complications were not reported. Consistent with Japan Clinical Oncology Group (JCOG) 1007 and CAIRO4,[21,22] the authors of the pooled SYNCRONOUS and CCRe-IV study concluded resection of the primary tumor before chemotherapy does not prolong survival in patients with newly diagnosed stage IV colon cancer with synchronous unresectable metastases.

Genitourinary

Prostate-specific membrane antigen PET response associates with radiographic progression-free survival following stereotactic ablative radiation therapy in oligometastatic castration-sensitive prostate cancer[23]

In an international multi-institutional retrospective study of 131 patients with oligometastatic castration-sensitive prostate cancer, defined as 3 or fewer lesions, this study evaluated prostate-specific membrane antigen (PSMA)-PET response following SABR as a marker for clinical outcomes. In the analysis, 261 metastases in 131 patients were treated with MFU of 29 months. Patients underwent PSMA-PET scans before and 3 to 6 months following treatment, with PSMA response defined using 30% or more decreased in SUV_{max}. Following SABR with MFU of 29 months, 78% of lesions had partial or CR. standardized uptake value (SUV) response was associated with improved LC (HR, 9.97; 95% CI, 3.92-25.4; $P < .01$) and radiographic PFS (HR, 0.49; CI, 0.26-0.92; $P = .03$). Additionally, patients with PSMA response had improved metastases-free survival (HR, 0.24; CI, 0.07-0.85; $P = .03$). This study suggests PSMA PET as a potential radiographic biomarker for radiographic PFS in patients with oligometastatic castration-sensitive prostate cancer following SABR. While further studies are needed, PSMA-PET could potentially be used to help guide treatment response and clinical management in the future.

Phase II, double-blind, randomized study of salvage radiation therapy (SRT) plus enzalutamide or placebo for high-risk PSA-recurrent prostate cancer after radical prostatectomy: The SALV-ENZA trial[24]

In a phase 2 double-blind randomized study in men with biochemically recurrent prostate cancer after radical prostatectomy, 86 patients were randomized to SRT plus either 6 months of enzalutamide or placebo. Trial arms were balanced according to surgical margin status (R0 vs R1), Prostate-Specific Antigen (PSA) before salvage (PSA

greater or less than 0.5 ng/mL), and pathologic Gleason score (7 vs ≥8). Patients were treated with SRT (66.6-70.2 Gy) to the prostate bed alone after initiating study drug for 2 months. Primary outcome was freedom from PSA progression. MFU was 34 months, median pretreatment PSA was 0.3 (range, 0.06-4.6 ng/mL), 65% had evidence of extraprostatic disease, 45% had Gleason score of ≥8, and 50% of patients had positive surgical margins. Two-year freedom from PSA progression was significantly improved with ENZA versus placebo (87.1% vs 68.1%; HR, 0.40; 95% CI, 0.17-0.92; $P = .026$). In subgroup analyses, there was a significant benefit of ENZA in men with pT3 disease (HR, 0.19; 95% CI, 0.05-0.67) versus pT2 disease (HR, 1.29; 95% CI, 0.34-4.81), with P value of interaction = .031. For men with PSA recurrent high-risk prostate disease, SRT plus ENZA appears to delay PSA progression relative to SRT alone with unknown impact on distant metastases or survival. One limitation of the study was pelvic nodal irradiation was not performed regardless of disease characteristics or nodal risk.

Impact of PSMA PET/CT on prostate cancer salvage radiotherapy management: Results from the prospective randomized phase 3 trial [PSMA SRT NCT03582774][25]

In a prospective randomized controlled phase 3 trial, 193 patients who were planned to undergo salvage RT for recurrent prostate cancer were randomized to undergo pretreatment evaluation with conventional imaging or PSMA PET/CT. Following imaging evaluation, treatment plans for before imaging and after treatment were evaluated to determine how imaging altered treatment plan. Changes were classified as either major (change of Androgen Deprivation Therapy (ADT) duration >3 months, change of standard RT volumes, targets delineated outside standard RT field, and initiation of advanced systemic therapy [novel ADT agents, chemotherapy]), minor (simultaneous integrated boost (SIB) within RT fields), or no changes. Following completion of enrollment, initial RT plan and delivered RT plan were available in 100% of patients. The median time from prostatectomy was 20.3 months (1.4-245 months) and median PSA was 0.3 ng/mL (0.1-29.9 ng/mL). In the PSMA group, 38% of patients had positive scans, with 12% outside the pelvis and 20% in the pelvic lymph nodes. Nine percent of patients received advanced systemic therapy compared with 1% in the control ($P = .044$). In the PSMA versus control group, there were major changes in 44% of patients versus 22% of patients, respectively ($P = .004$), with 71% of major changes in the PSMA group related to PSMA PET findings. Regarding minor changes, there were 7% of patients versus 0% of patients with changes, respectively. This study suggests significant changes in treatment planning for salvage radiation following PSMA PET in recurrent prostate cancer.

Head and Neck

Radiotherapy alone versus concurrent chemoradiotherapy in intermediate risk nasopharyngeal carcinoma: A multicentre, open-label, noninferiority, randomised phase III trial[26]

This single-country (China), multi-institutional phase 3 noninferiority RCT assessed the benefit of adding chemotherapy (cisplatin 100 mg/m^2 every 3 weeks) concurrently with RT for intermediate-risk (T1-2, N1, or T2-3N0) nasopharyngeal carcinoma (NPC). Patients were excluded if lymph node size >3 cm, positive lymph node level IV or lower, or pretherapy plasma EBV DNA >4000. A total of 341 patients were randomized to RT or CRT. With an MFU of 41 months, noninferiority of RT alone was established in the primary endpoint of failure-free survival in the 3-year intention-to-treat (90.7% vs 92.1%; P-noninferiority = .00017) and per-protocol (90.3% vs 92.1%; P-noninferiority = .00014) analyses. No differences were noted in OS (>98%), locoregional recurrence (LRR) (<6%), or distant metatases (DM) (<5%). Patients receiving chemotherapy developed significantly higher grade 3 to 4 toxicity, including vomiting, anorexia, mucositis, and weight loss. These results suggest that RT alone may be sufficient for well-selected intermediate-risk NPC.

Nimotuzumab plus chemoradiotherapy versus placebo plus chemoradiotherapy in patients with locally advanced nasopharyngeal carcinoma (NPC): A prospective, randomized-controlled, double-blinded, multicenter phase III clinical trial[27]

Epidermal growth factor receptor (EGFR) is highly expressed and prognostic in most NPC. This phase 3 RCT investigated the efficacy and safety of adding the EGFR inhibitor nimotuzumab (200 mg weekly for 7-8 weeks) to CRT in patients with locally advanced NPC. A total of 482 patients were enrolled (3:1 for nimotuzumab). The addition of nimotuzumab significantly improved the 5-year OS (76.9% vs 64.3%; $P = .042$) in the entire cohort. However, among patients treated per-protocol, there was no improvement noted in 5-year OS (75.7% vs 64.3%; $P = .183$). On multivariate analysis of the entire cohort, the OS benefit was confined to those who received 3-dimensional conformal

RT but not intensity modulated RT (IMRT). As such, the addition of nimotuzumab is not recommended in the modern era of IMRT.

Reduced-dose radiotherapy for pretreatment EBV DNA selected low-risk stage III nasopharyngeal carcinoma: A single-arm, phase II trial[28]

This single-arm, single-institution phase 2 trial aimed to de-escalate RT dose for select low-risk (EBV <4000) patients with stage III NPC based on response to induction chemotherapy. Patients received 2 cycles of TPF and those with a complete/partial response and undetectable EBV DNA levels subsequently received concurrent CRT (60 Gy IMRT; cisplatin 100 mg/m^2 every 3 weeks). Of 215 enrolled patients, 116 (54%) were able to receive lower dose IMRT. In these patients, the 2-year PFS, OS, locoregional recurence free survival (LRRFS,) and distant metastasis–free survival were 94%, 100%, 95%, and 97%, respectively. The most common toxicity during RT was grade 1 to 2 nausea (61%). The most common acute grade 3 to 4 toxicities were leucopenia (14%), neutropenia (14%), mucositis (11%), and pain (13%). No grade 3+ long-term side effect was observed. All quality of life (QOL) domains returned to baseline with the exception of xerostomia and sticky saliva. This study suggests RT de-escalation may be possible for a select group of patients with low-risk stage III NPC following a favorable response to induction chemotherapy.

An open-label, noninferiority phase III RCT of weekly versus three weekly cisplatin and radical radiotherapy in locally advanced head and neck squamous cell carcinoma (ConCERT trial)[29]

Cisplatin 100 mg/m2 every 3 weeks is considered the standard of care in locally advanced head and neck squamous cell carcinoma (LAHNSCC) receiving definitive concurrent CRT; however, many prefer a weekly cisplatin regimen of 40 mg/m^2 because of an assumed more favorable side effect profile. Indeed, this has been shown in the postoperative setting; however, it has not been prospectively tested in the intact setting until this noninferiority, phase 3 RCT.[30] A total of 278 patients were randomized. The primary sites included oropharynx (59.6%), larynx (17.5%), hypopharynx (11.6%), and oral cavity (11.6%). The tumor, nodes, metastases (TNM) stage was stage III (29.1%), stage IVA (50.5%), and stage IVB (20.4%). The every-3-weeks cisplatin arm had significantly higher treatment interruptions, hospitalizations, use of additional intravenous (IV) fluids, mucositis, myelosuppression, renal toxicity, vomiting, and hyponatremia. The weekly cisplatin regimen was found to be noninferior for 2-year locoregional control (LRC), PFS, and OS. This study supports the use of weekly cisplatin as the preferred agent for patients with LAHNSCC undergoing definitive concurrent CRT.

Results of phase 3 randomized trial for use of docetaxel as a radiosensitizer in patients with head and neck cancer unsuitable for cisplatin-based chemoradiation[31]

There are limited category 1 systemic therapy options for cisplatin-ineligible patients receiving definitive CRT for LAHNSCC. This phase 3 RCT randomized 356 patients to RT ± docetaxel 15 mg/m^2 weekly up to 7 cycles. The addition of docetaxel significantly improved the 2-year DFS (42% vs 30%), median OS (25.5 vs 15.3 months), and 2-year OS (50.8% vs 41.7%). Greater than any grade 3+ side effects were noted in the docetaxel arm (81.6% vs 58%), particularly in terms of mucositis (49.7% vs 22.2%), odynophagia (52.5% vs 33.5%), and dysphagia (49.7% vs 33%). At 6 months, the addition of docetaxel did not lead to a worsening of QOL based on assessments in Trial Outcome Index as well Functional Assessment of Cancer Therapy - General (FACT-G). Based on these results, concurrent docetaxel represents a new standard of care for cisplatin-ineligible LAHNSCC.

ROMAN: Phase 3 trial of avasopasem manganese (GC4419) for severe oral mucositis (SOM) in patients receiving chemoradiotherapy (CRT) for locally advanced, nonmetastatic head and neck cancer (LAHNC)[32]

Oral mucositis is a common and sometimes severe adverse effect of CRT in LAHNC. In later stages, mucositis can be so limiting that enteral feeding may be required. Pathophysiologically, oral mucositis development is related to an RT-induced burst of superoxide. Abasopasem (GC4419) is an investigational drug designed to convert superoxide to hydrogen peroxide, which may protect normal cells from RT-induced side effects. This double-blind placebo-controlled trial (3:2) investigated the impact of Abasopasem on reducing grade 3 to 4 oral mucositis in 407 patients with LAHNC undergoing CRT. The authors found a statistically significant 16% relative reduction in severe oral mucositis incidence (54% vs 64%), onset (49 vs 38 days from CRT), and duration (median, 8 vs 18

days) with the use of Abasopasem. No significant drug-induced side effects were reported. This represents significant progress in this setting given the lack of United States–approved drugs to reduce severe oral mucositis in LAHNC.

Effectiveness of adjuvant chemoradiotherapy for oral cavity squamous cell carcinoma with minor and major extranodal extension: A multi-institutional consortium study[33]

Extranodal extension is one of the indications for adjuvant CRT following surgical resection of oral cavity squamous cell carcinomas. Recent pathologic guidelines recommend stratifying extranodal extension (ENE) into minor (≤2 mm) or major (>2 mm). There is a suggestion that the addition of chemotherapy to RT may not improve outcomes in minor ENE. This large, multinational, multi-institutional cohort study aimed to evaluate this further. A total of 764 patients with surgically resected T1-4, N1-3, M0 oral cavity cancer with pathologic nodal disease who were treated between 2005 and 2018 were included in this analysis. Of these, 126 (16%) and 242 (32%) had minor and major ENE, respectively. Adjuvant CRT was administered to 40.5% and 47.5% of patients with minor and major ENE, respectively. The receipt of chemotherapy with RT was associated with improved OS in patients with major ENE but not minor ENE. This finding persisted after propensity score matched analysis. This study suggests that there may be a subgroup of patients with postoperative oral cavity tumors with ENE in whom treatment intensification with the addition of chemotherapy to RT may not be beneficial.

Lymphoma

First-line brentuximab vedotin plus chemotherapy to improve overall survival in patients with stage III/IV classical Hodgkin lymphoma: An updated analysis of ECHELON-1[34]

ECHELON-1 was a phase 3 trial involving 1334 adult patients with stage III to IV Hodgkin lymphoma (HL). Patients were randomized to receive up to 6 cycles of doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD) versus brentuximab vedotin + AVD [A+AVD], independent of interim PET/CT status. Approximately 10% of patients in each arm were Deauville 4-5 at the completion of treatment and were allowed to proceed without receipt of RT. The number of patients with initially bulky disease was not reported, and these patients were not required to receive RT. The primary endpoint was modified PFS, where modified PFS events were time to progression, death, or noncomplete response (Deauville 3-5) and use of subsequent anticancer therapy, including RT. At an MFU of 73 months, OS significantly favored A+AVD (HR, 0.59; CI, 0.40-0.88), with an estimated 6-year OS of 89% with ABVD and 93.9% with A+AVD. The 6-year PFS estimate was 74.5% with ABVD and 82.3% with A+AVD. Approximately 22% of patients received subsequent anticancer therapy, with 8% receiving RT and 14% receiving chemotherapy-based approaches. Treatment-emergent peripheral neuropathy was an initial concern in the brentuximab vidotin arm, with grade 2+ peripheral neuropathy of 9% with ABVD and 20% with A+AVD. Fortunately, peripheral neuropathy continued to resolve or improve in around 86% of cases. The authors conclude A+AVD results in a statistically significant 41% reduction in the risk of death versus ABVD, with a manageable safety profile.

Brentuximab vedotin and association with event-free survival (EFS) in children with newly diagnosed high-risk Hodgkin lymphoma (HL): A report from the Children's Oncology Group phase 3 study AHOD1331 (NCT 02166463)[35]

AHOD1331 was a phase 3 trial enrolling 587 eligible patients aged 2 to 21 years with stage IIB, IIIB, IVA, and IVB HL. Stage III to IV disease comprised the majority (79%) of the patient cohort. Patients were randomized to receive up to 5 cycles of brentuximab vedotin (Bv) with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide (Bv-AVE-PC) or the standard pediatric dose intensive regimen ABVE-PC, inclusive of bleomycin. RT was viewed quite differently than ECHELON-1, where prior data from AHOD 0031 suggested poor outcomes for patients with positive interim PET/CT (PET2 Deauville 4-5; slow responding lesions) or with large mediastinal masses.[36] Therefore, RT was delivered to all bulky mediastinal lesions (35%) and slow responding lesions (19%), resulting in involved site RT receipt in approximately 54% of patients on each arm (compared with 8% receiving RT on ECHELON-1). At an MFU of 42 months, 3-year EFS by intention-to-treat analysis was 82.5% with ABVE-PC and 92.1% with Bv-AVE-PC. Relapse rate was 17% with ABVE-PC and 7% with Bv-AVE-PC. There was no difference in grade 3 to 4 events observed between arms, and only 19% of patients experienced grade 3+ neuropathy by the Balis pediatric neuropathy scale. The authors concluded Bv-AVE-PC has superior efficacy to ABVE-PC for pediatric patients with high-risk HL. These 2 trials highlight key differences in RT utilization for advanced HL, with a more liberal approach to incorporating RT in the pediatric population (eg, PET2 Deauville 4-5 and mediastinal lesions with initial bulk) than in the adult population. However, it is

unclear if more liberal use of RT in AHOD1331 was associated with lower relapse risk compared with ECHELON-1 and one should be wary of cross comparison between these heterogeneous trial populations and intervention strategies.

Thoracic

Comparison of quality of life in patients randomized to high-dose once daily (QD) thoracic radiotherapy (TRT) with standard twice daily (bid) TRT in limited stage small cell lung cancer (LS-SCLC) on CALGB 30610 (Alliance, Sub-study CALGB 70702)[37]

Cancer and Leukemia Group B (CALGB) 30610 was a randomized trial of QD RT versus standard-of-care twice-daily (bid) RT. Although the trial was unable to meet its primary endpoint of improved OS with high-dose QD RT, it did find numerically comparable efficacy and toxicity outcomes between the 2 arms. Here, the authors presented results from a planned substudy (CALGB 70702) investigating patient QOL, as determined by physical symptoms, physical functioning, and psychological state, between the QD and bid regimens. A total of 417 patients participated in the CALGB 70702 substudy. The completion rate of the questionnaires was 87% at baseline and 71% at week 52. Patients in the QD arm noted better QOL scores, with a smaller reduction in the mean score for FACT-L, FACT-L TOI, and EQ-D5 index than those in the bid regimen, though this was primarily at 3 weeks. Mean increase in the acute esophagitis score (1.06 vs 2.89; $P < .001$) and difficulty swallowing (0.39 vs 1.14; $P < .001$) was significantly greater in the bid arm at week 3. Lastly, across visits, a higher percentage of patients in the bid arm versus those on the QD arm felt that treatment was inconvenient, 33% (116/352 assessments) versus 26% (96/376 assessments) (χ^2 $P = .03$). In conclusion, both regimens were well tolerated with a short-term acute logistical convenience and QOL advantage favoring QD.

Improved survival from early combined radiotherapy: A phase II clinical study and underlying mechanisms of delaying EGFR-TKI acquired resistance in patients with advanced lung cancer[38]

The role of SBRT in the setting of stage IV NSCLC has continued to evolve because of improvements in PFS and OS with newer systemic agents; however, the representation of patients with EGFR-mutated NSCLC in trials has been limited. In this study, researchers from Tongji Hospital evaluated the safety and efficacy of adding SBRT to patients receiving EGFR tyrosine kinase inhibitors (TKI) who had achieved stable disease or partial response. Between March 2015 and March 2018, 61 patients who met the inclusion criteria were randomized to TKI alone or TKI + SBRT. Among the total cohort, 30 (49.1%) specifically had a T790M with no differences noted among cohorts. The median PFS and OS of the TKI and TKI + SBRT cohorts was 9.0 versus 17.6 months ($P = .016$) and 23.2 versus 33.6 months ($P = .026$), respectively. Treatment-related adverse events were generally safe and controllable. Furthermore, the researchers performed xenograft experiments in mice that showed SBRT led to superior tumor regression and timing of EGFR TKI resistance. These results add to the recently published SINDAS trial from Sichuan Provincial People's Hospital, which showed improved PFS and OS with the addition of early upfront SBRT in oligometastatic EGFR-mutated NSCLC receiving TKIs.[39] One caveat of both trials is that they were in the pre-Osimertinib era. Trials evaluating the addition of SBRT in patients receiving Osimertinib are currently ongoing.

Two-year update from KEYNOTE-799: Pembrolizumab plus concurrent chemoradiation therapy (cCRT) for unresectable, locally advanced, stage III NSCLC[40]

At the 2022 American Society of Clinical Oncology meeting, the investigators reported updated results of KEYNOTE-799, a nonrandomized 2-cohort trial of adding pembrolizumab with cCRT in locally advanced stage III NSCLC, following an additional year of follow-up. Cohort A (squamous/nonsquamous) received 1 cycle of carboplatin (area under the curve, 6 mg/mL/min), paclitaxel (200 mg/m^2), and pembrolizumab (200 mg), followed by weekly carboplatin (area under the curve, 2 mg/mL/min) and paclitaxel (45 mg/m^2) for 6 weeks and 2 cycles of pembrolizumab plus standard thoracic RT. Cohort B (nonsquamous) received 3 cycles of cisplatin (75 mg/m^2), pemetrexed (500 mg/m^2), and pembrolizumab (200 mg) every 3 weeks and thoracic RT in cycles 2 and 3. Patients then received 14 additional cycles of pembrolizumab. In this update, the overall response rate (ORR) was 71.4% in cohort A and 75.5% in cohort B. The median duration of response and OS were not reached in both cohorts. The median PFS was 30.6 months and not reached in cohort A and B, respectively. The ORR in patients with Programmed death-ligand 1 (PD-L1) tumor proportion score (TPS) <1% and PD-L1 TPS ≥1% was 66.7% and 77.3% in cohort A and 78.6% and 72.5% in cohort B. No difference in ORR was seen based on histology. Grade ≥3 pneumonitis occurred in 16 patients (7.5%) overall; 9 patients (8.0%) in cohort A and 7 (6.9%) in cohort B. In conclusion, updated results continue to show that

pembrolizumab plus cCRT demonstrates robust and durable responses, regardless of PD-L1 TPS and tumor histology, promising survival outcome and manageable safety in patients with previously untreated, locally advanced stage III NSCLC.

Consolidation nivolumab plus ipilimumab or nivolumab alone following concurrent chemoradiation for patients with unresectable stage III non-small cell lung cancer: BTCRC LUN 16-081[41]

Though the PACIFIC trial confirmed improved survival outcomes with consolidation immunotherapy (IO) therapy following cCRT, the appropriate duration of therapy and possible combinatory regimens (PD-(L)-1/CTLA-4) remains an open question. In BTCRC LUN 16-081, patients with unresectable stage IIIA/IIIB NSCLC who completed cCRT were randomized to up to 6 months of adjuvant nivolumab (N) 480 mg IV every 4 weeks (arm A) or the combination of N 3 mg/kg IV every 2 weeks and ipilimumab (IPI) 1 mg/kg IV every 6 weeks (arm B). The primary endpoint was to evaluate PFS at 18 months, which was compared with historical controls of CRT alone for arm A (30%) and CRT followed by durvalumab for arm B (44%). The MFU was roughly 24 months for both arms. The 18-month and median PFS was 62.3% and 25.8 months on arm A and 67% and 25.4 months on arm B, respectively. The median OS was not reached on either arm. The estimated 18- and 24-month OS rates were 82.1% and 76.6% for A and 85.5% and 82.8% for B, respectively. Overall and grade ≥3 treatment-related adverse events on arm A and B were 72.2% and 38.9% and 80.4% and 52.9%, respectively. The rate of grade ≥2 and grade ≥3 pneumonitis was 22.2% and 9.3% in arm A and 29.4% and 15.7% in arm B. In conclusion, both N and N + IPI of only 6-month duration demonstrated improved 18-month PFS compared with historical controls. Treatment toxicity was consistent with prior studies with the combination of N + IPI resulting in a higher incidence of treatment related adverse effects (trAE)s than N alone.

Sarcoma

Outcomes following preoperative chemoradiation +/- pazopanib in non-rhabdomyosarcoma soft tissue sarcoma (NRSTS): A report from Children's Oncology Group (COG) and NRG Oncology[42]

ARST1321 was a phase 2 study designed to compare the near complete pathologic response rate (≥90% necrosis) following preoperative CRT ± pazopanib in children and adults with intermediate/high-risk chemotherapy-sensitive extremity/trunk nonrhabdomyosarcoma Soft tissue sarcoma (STS). Enrollment was stopped early following a predetermined interim analysis showing significantly higher near-pathologic response rate with the addition of pazopanib. The authors now report the outcomes data for this cohort. A total of 85 eligible patients were enrolled and randomized. With a median survivor follow-up of 3.3 years, there was no difference seen in 3-year EFS or 3-year OS between those who received or did not receive pazopanib. This study suggests that near complete pathologic response rate may not be a good surrogate marker of outcomes in this patient population.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2022.101107.

References

1. Shukla U, Chhabra A, Wazer D, Chowdhary M. American Society of Clinical Oncology 2021 annual meeting highlights for radiation oncologists. *Adv Radiat Oncol*. 2022;7: 100779.
2. Chmura SJ, Winter KA, Woodward WA, et al. NRG-BR002: A phase IIR/III trial of standard of care systemic therapy with or without stereotactic body radiotherapy (SBRT) and/or surgical resection (SR) for newly oligometastatic breast cancer (NCT02364557). *J Clin Oncol*. 2022;40(16 suppl):1007.
3. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy for the comprehensive treatment of oligometastatic cancers: Long-term results of the SABR-COMET phase II randomized trial. *J Clin Oncol*. 2020;38:2830-2838.
4. Tsai CJ, Yang JT, Guttmann DM, et al. Consolidative Use of Radiotherapy to Block (CURB) oligoprogression – interim analysis of the first randomized study of stereotactic body radiotherapy in patients with oligoprogressive metastatic cancers of the lung and breast. *Int J Radiat Oncol Biol Phys*. 2021;111:1325-1326.
5. Whelan TJ, Smith S, Nielsen TO, et al. LUMINA: A prospective trial omitting radiotherapy (RT) following breast conserving surgery (BCS) in T_1N_0 luminal A breast cancer (BC). *J Clin Oncol*. 2022;40 (17 suppl):LBA501.
6. Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: Long-term follow-up of CALGB 9343. *J Clin Oncol*. 2013;31:2382-2387.
7. Blamey RW, Bates T, Chetty U, et al. Radiotherapy or tamoxifen after conserving surgery for breast cancers of excellent prognosis: British Association of Surgical Oncology (BASO) II trial. *Eur J Cancer*. 2013;49:2294-2302.
8. Chowdhary M, Chhabra AM, Jhawar SR. Omission of radiotherapy in older adults with early-stage breast cancer—reply. *JAMA Oncol*. 2021;7:1398.
9. Chowdhary M, Chhabra AM, Jhawar SR. Is it time to reevaluate radiotherapy omission in older patients with favorable early-stage breast cancer? *JAMA Oncol*. 2021;7:965.

10. Yang JT, Wijetunga NA, Pentsova E, et al. Phase II randomized study comparing proton craniospinal irradiation with photon involved-field radiotherapy for patients with solid tumor leptomeningeal metastasis. *J Clin Oncol*. 2022;40(16 suppl):2000.
11. Yang JT, Wijetunga NA, Pentsova E, et al. Randomized phase II trial of proton craniospinal irradiation versus photon involved-field radiotherapy for patients with solid tumor leptomeningeal metastasis [e-pub ahead of print]. *J Clin Oncol*. https://doi.org/10.1200/JCO.22.01148, accessed July 18, 2022.
12. Gardner M, Stahl F, Dietrich J, et al. A controlled comparison of cerebral volume loss after brain irradiation with proton versus photon radiotherapy. *J Clin Oncol*. 2022;40(16 suppl):2017.
13. Cercek A, Lumish MA, Sinopoli JC, et al. Single agent PD-1 blockade as curative-intent treatment in mismatch repair deficient locally advanced rectal cancer. *J Clin Oncol*. 2022;40(17 suppl):LBA5.
14. Gerard JP, Barbet NN, Pacé-Loscos T, et al. Contact x-ray brachytherapy (Papillon) in addition to chemoradiotherapy to improve organ preservation in early cT2-T3 rectal adenocarcinoma: The 3-year results of OPERA randomized trial (NCT02505750). *J Clin Oncol*. 2022;40(16 suppl):3512.
15. Bach SP, de Wilt JHW, Peters F, et al. STAR-TREC phase II: Can we save the rectum by watchful waiting or transanal surgery following (chemo)radiotherapy versus total mesorectal excision for early rectal cancer? *J Clin Oncol*. 2022;40(16 suppl):3502.
16. Jensen LH, Risum S, Nielsen JD, et al. Curative chemoradiation for low rectal cancer: Primary clinical outcomes from a multicenter phase II trial. *J Clin Oncol*. 2022;40(17 suppl):LBA3514.
17. Stewart AJ, van Limbergen EJ, Gerard JP, et al. GEC ESTRO ACROP consensus recommendations for contact brachytherapy for rectal cancer. *Clin Transl Radiat Oncol*. 2022;33:15-22.
18. Yuval JB, Verheij FS, Lin ST, et al. Clinical and radiological predictors of organ preservation in patients with rectal cancer treated with total neoadjuvant therapy. *J Clin Oncol*. 2022;40(16 suppl):3619.
19. Fietkau R, Ghadimi M, Grützmann R, et al. Randomized phase III trial of induction chemotherapy followed by chemoradiotherapy or chemotherapy alone for nonresectable locally advanced pancreatic cancer: First results of the CONKO-007 trial. *J Clin Oncol*. 2022;40(16 suppl):4008.
20. Rahbari NN, Biondo S, Feißt M, et al. Randomized clinical trial on resection of the primary tumor versus no resection prior to systemic therapy in patients with colon cancer and synchronous unresectable metastases. *J Clin Oncol*. 2022;40(17 suppl):LBA3507.
21. Moritani K, Kanemitsu Y, Shida D, et al. A randomized controlled trial comparing primary tumour resection plus chemotherapy with chemotherapy alone in incurable stage IV colorectal cancer: JCOG1007 (iPACS study). *Jpn J Clin Oncol*. 2020;50:89-93.
22. van der Kruijssen DEW, Elias SG, Vink GR, et al. Sixty-day mortality of patients with metastatic colorectal cancer randomized to systemic treatment vs primary tumor resection followed by systemic treatment. *JAMA Surg*. 2021;156:1093.
23. Sutera P, Deek M, Guler OC, et al. Prostate-specific membrane antigen PET response associates with radiographic progression-free survival following stereotactic ablative radiation therapy in oligometastatic castration-sensitive prostate cancer. *J Clin Oncol*. 2022;40(16 suppl):5011.
24. Tran PT, Lowe K, Wang H, et al. Phase II, double-blind, randomized study of salvage radiation therapy (SRT) plus enzalutamide or placebo for high-risk PSA-recurrent prostate cancer after radical prostatectomy: The SALV-ENZA trial. *J Clin Oncol*. 2022;40(16 suppl):5012.
25. Armstrong WR, Kishan AU, Booker KM, et al. Impact of PSMA PET/CT on prostate cancer salvage radiotherapy management: Results from the prospective randomized phase 3 trial [PSMA SRT NCT03582774]. *J Clin Oncol*. 2022;40(16 suppl):5028.
26. Ma J, Tang LL, Guo R, Chen L. Radiotherapy alone versus concurrent chemoradiotherapy in intermediate risk nasopharyngeal carcinoma: A multicentre, open-label, noninferiority, randomised phase III trial. *J Clin Oncol*. 2022;40(16 suppl):6000.
27. Sun Y, Hu C, Lin Q. Nimotuzumab plus chemoradiotherapy versus placebo plus chemoradiotherapy in patients with locally advanced nasopharyngeal carcinoma (NPC): A prospective, randomized-controlled, double-blinded, multicenter phase III clinical trial. *J Clin Oncol*. 2022;40(16 suppl):6001.
28. Mai HQ, Yang JH, Guo SS, et al. Reduced-dose radiotherapy for pretreatment EBV DNA selected low-risk stage III nasopharyngeal carcinoma: A single-arm, phase II trial. *J Clin Oncol*. 2018;40:6002.
29. Sharma A, Kumar M, Bhasker S, et al. An open-label, noninferiority phase III RCT of weekly versus three weekly cisplatin and radical radiotherapy in locally advanced head and neck squamous cell carcinoma (ConCERT Trial). *J Clin Oncol*. 2022;40:6004.
30. Kiyota N, Tahara M, Mizusawa J, et al. Weekly cisplatin plus radiation for postoperative head and neck cancer (JCOG1008): A multicenter, noninferiority, phase II/III randomized controlled trial. *J Clin Oncol*. 2022;40:1980.
31. Patil VM, Noronha V, Menon S, et al. Results of phase 3 randomized trial for use of docetaxel as a radiosensitizer in patients with head and neck cancer unsuitable for cisplatin-based chemoradiation. *J Clin Oncol*. 2022;40:LBA6003.. LBA6003.
32. Anderson CM, Lee CM, Kelley JR, et al. ROMAN: Phase 3 trial of avasopasem manganese (GC4419) for severe oral mucositis (SOM) in patients receiving chemoradiotherapy (CRT) for locally advanced, nonmetastatic head and neck cancer (LAHNC). *J Clin Oncol*. 2022;40:6005.
33. Manojlovic Kolarski M, Su J, Weinreb I, et al. Effectiveness of adjuvant chemoradiotherapy for oral cavity squamous cell carcinoma with minor and major extranodal extension: A multi-institutional consortium study. *J Clin Oncol*. 2022;40:6010.
34. Ansell SM, Connors JM, Radford JA, et al. First-line brentuximab vedotin plus chemotherapy to improve overall survival in patients with stage III/IV classical Hodgkin lymphoma: An updated analysis of ECHELON-1. *J Clin Oncol*. 2022;40(16 suppl):7503.
35. Castellino SM, Pei Q, Parsons SK, et al. Brentuximab vedotin and association with event-free survival (EFS) in children with newly diagnosed high-risk Hodgkin lymphoma (HL): A report from the Children's Oncology Group phase 3 study AHOD1331 (NCT 02166463). *J Clin Oncol*. 2022;40(16 suppl):7504.
36. Charpentier AM, Friedman DL, Wolden S, et al. Predictive factor analysis of response-adapted radiation therapy for chemotherapy-sensitive pediatric Hodgkin lymphoma: Analysis of the Children's Oncology Group AHOD 0031 trial. *Int J Radiat Oncol Biol Phys*. 2016;96:943-950.
37. Ganti AK, Dueck AC, Fruth B, et al. Comparison of quality of life in patients randomized to high-dose once daily (QD) thoracic radiotherapy (TRT) with standard twice daily (BID) TRT in limited stage small cell lung cancer (LS-SCLC) on CALGB 30610 (Alliance, Substudy CALGB 70702). *J Clin Oncol*. 2022;40(16 suppl):8504.
38. Zhang L, Peng P, Gong J, et al. Improved survival from early combined radiotherapy: A phase II clinical study and underlying mechanisms of delaying EGFR-TKI acquired resistance in patients with advanced lung cancer. *J Clin Oncol*. 2022;40(16 suppl):9114.
39. Wang XS, Bai YF, Verma V, et al. Randomized trial of first-line tyrosine kinase inhibitor with or without radiotherapy for synchronous oligometastatic *EGFR*-mutated non-small cell lung cancer [e-pub ahead of print]. *JNCI: J Natl Cancer Inst*. https://doi.org/10.1093/jnci/djac015, accessed July 18, 2022.

40. Reck M, Lee KH, Frost N, et al. Two-year update from KEYNOTE-799: Pembrolizumab plus concurrent chemoradiation therapy (cCRT) for unresectable, locally advanced, stage III NSCLC. *J Clin Oncol*. 2022;40(16 suppl):8508.
41. Durm GA, Mamdani H, Althouse SK, et al. Consolidation nivolumab plus ipilimumab or nivolumab alone following concurrent chemoradiation for patients with unresectable stage III non-small cell lung cancer: BTCRC LUN 16-081. *J Clin Oncol*. 2022;40(16 suppl):8509.
42. Weiss AR, Chen YL, Scharschmidt T, et al. outcomes following preoperative chemoradiation +/- pazopanib in non-rhabdomyosarcoma soft tissue sarcoma (NRSTS): A report from Children's Oncology Group (COG) and NRG Oncology. *J Clin Oncol*. 2022;40:11504.