FLORIDA CANCER SPECIALISTS & Research Institute

TOP ARTICLES OF THE MONTH

OCTOBER 2021 | Lucio N. Gordan, MD

1. Immunotherapy in Patients With Locally Advanced Esophageal Carcinoma: ASCO Treatment of Locally Advanced Esophageal Carcinoma Guideline Rapid Recommendation Update

Manish A. Shah , MD; Wayne L. Hofstetter, MD; and Erin B. Kennedy , MHSc; for the Locally Advanced Esophageal Carcinoma Guideline Expert Panel

ABSTRACT

In 2020, ASCO published a guideline on the management of locally advanced esophageal cancer.1 The CheckMate 577 double-blind, placebo-controlled, phase III randomized controlled trial (RCT) was recently reported, evaluating the efficacy of the addition of the checkpoint inhibitor nivolumab following neoadjuvant chemoradiotherapy (CRT) and surgery in patients with stage II/III esophageal carcinoma with residual disease (ie, patients who had viable disease in the surgical resection specimen after receiving CRT).2 The CheckMate 577 results provided a strong signal indicating the need to update the 2020 guideline recommendations.

METHODS

A targeted electronic literature search was conducted to identify any additional phase III RCTs of treatment options in this patient population. No additional RCTs were identified. The original guideline Expert Panel was reconvened to review new evidence from CheckMate 577 and to review and approve the revised recommendation.

EVIDENCE REVIEW

The RCT by Kelly et al2 included 794 patients with esophageal or gastroesophageal junction adenocarcinoma (71%) or esophageal squamous cell carcinoma (29%) and residual pathological disease after neoadjuvant CRT and an R0 resection. More than 50% of patients had lymph node–positive disease. The primary outcome, disease-free survival (DFS), was significantly improved for patients receiving neoadjuvant CRT + surgery and adjuvant nivolumab compared to CRT + surgery and adjuvant placebo (hazard ratio: 0.69; 96.4% CI, 0.56 to 0.86; P < .001). Treatment-related grade 3-4 adverse events were experienced by 13% versus 6% in the nivolumab and placebo groups, respectively (relative risk: 2.31; 95% CI, 1.35 to 3.96; P = .002). Using the GRADE methodology,3 study quality was downgraded from high to moderate because the number of events needed to report on secondary outcome overall survival has not yet been achieved. The DFS results were significant across both adenocarcinoma and squamous cell carcinoma subgroups.

2020 RECOMMENDATION

Choose

Prior to the publication of the CheckMate 577 data, the ASCO 2020 guideline for locally advanced esophageal cancer did not include recommendations for further treatment of patients with residual disease following resection and CRT. The previous standard of care for this patient population was surveillance.

2021 UPDATED RECOMMENDATION

Following neoadjuvant CRT and surgery, nivolumab should be offered to patients with locally advanced esophageal carcinoma with Eastern Cooperative Oncology Group status 0-1 who did not experience a pathological complete response (ie, with residual disease of at least ypT1 or ypN1 in resected specimens; Type: evidence-based, benefits outweigh harms; Evidence quality: moderate; Strength of recommendation: strong).

QUALIFYING STATEMENTS

Data are not available to support any recommendation for nivolumab following treatment with perioperative chemotherapy.

A post hoc analysis showed an hazard ratio for DFS of 0.62 (95% CI, 0.46 to 0.83; median DFS 29.4 v 10.2 months) in the subgroup of patients with programmed death-ligand 1 (PD-L1) combined positive score (CPS) of at least 5 (n = 371) and 0.89 (95% CI, 0.65 to 1.22; median DFS 16.3 v 11.1 months) in the subgroup of patients with PD-L1 CPS of < 5 (n = 295). This exploratory analysis suggests that future studies may define biomarkers, such as PD-L1 CPS, and/or a subgroup that will benefit from adjuvant nivolumab.

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2. Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial

John C Byrd, Peter Hillmen, Paolo Ghia, Arnon P Kater, Asher Chanan-Khan, Richard R Furman, Susan O'Brien, Mustafa Nuri Yenerel, Arpad Illés, Neil Kay, Jose A Garcia-Marco, Anthony Mato, Javier Pinilla-Ibarz, John F Seymour, Stephane Lepretre, Stephan Stilgenbauer, Tadeusz Robak, Wayne Rothbaum, Raquel Izumi, Ahmed Hamdy, Priti Patel, Kara Higgins, Sophia Sohoni, Wojciech Jurczak

ABSTRACT

Among Bruton's tyrosine kinase inhibitors, acalabrutinib has greater selectivity than ibrutinib, which we hypothesized would improve continuous therapy tolerability. We conducted an open-label, randomized, noninferiority, phase III trial comparing acalabrutinib and ibrutinib in patients with chronic lymphocytic leukemia (CLL).

METHODS

Patients with previously treated CLL with centrally confirmed del(17)(p13.1) or del(11)(q22.3) were randomly assigned to oral acalabrutinib 100 mg twice daily or ibrutinib 420 mg once daily until progression or unacceptable toxicity. The primary end point was independent review committee–assessed noninferiority of progression-free survival (PFS).

RESULTS

Overall, 533 patients (acalabrutinib, n = 268; ibrutinib, n = 265) were randomly assigned. At the data cutoff, 124 (46.3%) acalabrutinib patients and 109 (41.1%) ibrutinib patients remained on treatment. After a median follow-up of 40.9 months, acalabrutinib was determined to be noninferior to ibrutinib with a median PFS of 38.4 months in both arms (95% CI acalabrutinib, 33.0 to 38.6 and ibrutinib, 33.0 to 41.6; hazard ratio: 1.00; 95% CI, 0.79 to 1.27). All-grade atrial fibrillation/atrial flutter incidence was significantly lower with acalabrutinib versus ibrutinib (9.4% v 16.0%; P = .02); among other selected secondary end points, grade 3 or higher infections (30.8% v 30.0%) and Richter transformations (3.8% v 4.9%) were comparable between groups and median overall survival was not reached in either arm (hazard ratio, 0.82; 95% CI, 0.59 to 1.15), with 63 (23.5%) deaths with acalabrutinib and 73 (27.5%) with ibrutinib. Treatment discontinuations because of adverse events occurred in 14.7% of acalabrutinib-treated patients and 21.3% of ibrutinib-treated patients.

CONCLUSION

In this first direct comparison of less versus more selective Bruton's tyrosine kinase inhibitors in CLL, acalabrutinib demonstrated noninferior PFS with fewer cardiovascular adverse events.

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3. Comparison Between 5-Azacytidine Treatment and Allogeneic Stem-Cell Transplantation in Elderly Patients with Advanced MDS According to Donor Availability (VidazaAllo Study)

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ABSTRACT

In contrast to 5-azacytidine (5-aza), allogeneic stem-cell transplantation (HSCT) represents a curative treatment strategy for patients with myelodysplastic syndromes (MDS), but therapy-related mortality (TRM) limits its broader use in elderly patients with MDS. The present prospective multicenter study compared HSCT following 5-aza pretreatment with continuous 5-aza treatment in patients with higher-risk MDS age 55-70 years.

METHODS

One hundred ninety patients with a median age of 63 years were enrolled. Patients received 4-6 cycles of 5-aza followed by HLA-compatible HSCT after reduced-intensity conditioning or by continuous 5-aza if no donor was identified.

RESULTS

Twenty-eight patients did not fulfill inclusion criteria (n = 20), died (n = 2) withdrew informed consent (n = 5), or were excluded for an unknown reason (n = 1). 5-aza induction started in 162 patients, but only 108 (67%) were eligible for subsequent allocation to HSCT (n = 81) or continuation of 5-aza (n = 27) because of disease progression (n = 26), death (n = 12), or other reasons (n = 16). Seven percent died during 5-aza before treatment allocation. The cumulative incidence of TRM after HSCT at 1 year was 19%. The event-free survival and overall survival after 5-aza pretreatment and treatment allocation at 3 years were 34% (95% CI, 22 to 47) and 50% (95% CI, 39 to 61) after allograft and 0% and 32% (95% CI, 14 to 52) after continuous 5-aza treatment ($P < .0001$ and $P = .12$), respectively. Fourteen patients progressing after continuous 5-aza received a salvage allograft from an alternative donor, and 43% were alive at last follow-up.

CONCLUSION

In older patients with MDS, reduced-intensity conditioning HSCT resulted in a significantly improved event-free survival in comparison with continuous 5-aza therapy. Bridging with 5-aza to HSCT before is associated with a considerable rate of dropouts because of progression, mortality, and adverse events.

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4. Physical Activity Patterns and Relationships with Cognitive Function in Patients With Breast Cancer Before, During, and After Chemotherapy in a Prospective, Nationwide Study

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ABSTRACT

Physical activity (PA) is a promising intervention for cancer-related cognitive decline, yet research assessing its use during chemotherapy is limited. This study evaluated patterns of PA before, during, and after chemotherapy in patients with breast cancer and the association between PA and cognitive function.

METHODS

In a nationwide, prospective cohort study, we assessed PA (Aerobics Center Longitudinal Study PA measure) and perceived and objectively measured cognitive functioning (Functional Assessment of Cancer Therapy–Cognitive, Delayed Match to Sample, and Rapid Visual Processing measures) at prechemotherapy (T1), postchemotherapy (T2), and 6 months postchemotherapy (T3) in patients with breast cancer and cancer-free, age-matched controls at equivalent time points. Longitudinal linear mixed-effects models (LMMs) characterized PA changes over time between patients and controls, adjusting for demographic and clinical factors. LMMs further estimated the role of prechemotherapy PA and changes in PA during chemotherapy on cognitive changes over time.

RESULTS

Patients with stage I-IIIC breast cancer (n = 580; age M [standard deviation] = 53.4 [10.6] years) and controls (n = 363; age M [standard deviation] = 52.6 [10.3] years) were included. One third of patients met national PA guidelines at T1, dropping to 21% at T2 before rising to 37% at T3. LMMs revealed declines in PA from T1 to T2 in patients compared with controls (all $P < .001$). Patients meeting guidelines at T1 demonstrated better cognitive scores over time on the Functional Assessment of Cancer Therapy–Cognitive and Rapid Visual Processing (all $P < .05$), with similar patterns of objectively-measured cognitive function as controls. In patients, greater moderate-to-vigorous PA at the previous time point was significantly associated with better cognitive trajectories (all $P < .05$), and adherence to PA guidelines throughout chemotherapy was associated with better self-reported cognition ($P < .01$).

CONCLUSION

This nationwide study demonstrates that PA maintenance before and during chemotherapy is associated with better cognitive function immediately and 6 months after chemotherapy completion.

5. Gemcitabine Plus Cisplatin Versus Fluorouracil Plus Cisplatin as First-Line Therapy for Recurrent or Metastatic Nasopharyngeal Carcinoma: Final Overall Survival Analysis of GEM20110714 Phase III Study

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ABSTRACT

GEM20110714 (ClinicalTrials.gov identifier: NCT01528618), the first randomized, phase III study of systemic chemotherapy in recurrent or metastatic nasopharyngeal carcinoma (NPC), reported significant progression-free survival improvement with gemcitabine plus cisplatin (GP) versus fluorouracil plus cisplatin (FP; hazard ratio, 0.55; 95% CI, 0.44 to 0.68; P < .001). Data from the final analysis of overall survival (OS) are presented here.

METHODS

From February 2012 to October 2015, 362 patients were randomly assigned to receive either GP (gemcitabine 1 g/m2 once daily on days 1 and 8 and cisplatin 80 mg/m2 once daily on day 1; n = 181) or FP (fluorouracil 4 g/m2 in continuous intravenous infusion over 96 hours and cisplatin 80 mg/m2 once daily on day 1; n = 181) once every 21 days. The primary end point was progression-free survival, which has been previously reported; OS was a secondary end point.

RESULTS

After a median follow-up time of 69.5 months with GP and 69.7 months with FP, 148 (81.8%) and 166 (91.7%) deaths occurred in the GP and FP arms, respectively. The estimated hazard ratio for OS was 0.72 (95% CI, 0.58 to 0.90; two-sided P = .004). The median OS was 22.1 months (95% CI, 19.2 to 25.0 months) with GP versus 18.6 months (95% CI, 15.4 to 21.7 months) with FP. The OS probabilities at 1, 3, and 5 years were 79.9% versus 71.8%, 31.0% versus 20.4%, and 19.2% versus 7.8%, respectively. Poststudy therapy was administered in 51.9% and 55.2% of patients in the GP and FP arms, respectively.

CONCLUSION

Among patients with previously untreated advanced nasopharyngeal carcinoma, those who receive GP have longer OS than those receive FP. Gemcitabine plus cisplatin should be considered a preferred front-line option for these patients.

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6. Randomized Phase III Trial of Prophylactic Cranial Irradiation with or Without Hippocampal Avoidance for Small-Cell Lung Cancer (PREMER): A GICOR-GOECP-SEOR Study

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ABSTRACT

Radiation dose received by the neural stem cells of the hippocampus during whole-brain radiotherapy has been associated with neurocognitive decline. The key concern using hippocampal avoidance-prophylactic cranial irradiation (HA-PCI) in patients with small-cell lung cancer (SCLC) is the incidence of brain metastasis within the hippocampal avoidance zone.

METHODS

This phase III trial enrolled 150 patients with SCLC (71.3% with limited disease) to standard prophylactic cranial irradiation (PCI; 25 Gy in 10 fractions) or HA-PCI. The primary objective was the delayed free recall (DFR) on the Free and Cued Selective Reminding Test (FCSRT) at 3 months; a decrease of 3 points or greater from baseline was considered a decline. Secondary end points included other FCSRT scores, quality of life (QoL), evaluation of the incidence and location of brain metastases, and overall survival (OS). Data were recorded at baseline, and 3, 6, 12, and 24 months after PCI.

RESULTS

Participants' baseline characteristics were well balanced between the two groups. The median follow-up time for living patients was 40.4 months. Decline on DFR from baseline to 3 months was lower in the HA-PCI arm (5.8%) compared with the PCI arm (23.5%; odds ratio, 5; 95% CI, 1.57 to 15.86; P = .003). Analysis of all FCSRT scores showed a decline on the total recall (TR; 8.7% v 20.6%) at 3 months; DFR (11.1% v 33.3%), TR (20.3% v 38.9%), and total free recall (14.8% v 31.5%) at 6 months, and TR (14.2% v 47.6%) at 24 months. The incidence of brain metastases, OS, and QoL were not significantly different.

CONCLUSION

Sparing the hippocampus during PCI better preserves cognitive function in patients with SCLC. No differences were observed with regard to brain failure, OS, and QoL compared with standard PCI.

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7. Chemotherapy with or without avelumab followed by avelumab maintenance versus chemotherapy alone in patients with previously untreated epithelial ovarian cancer (JAVELIN Ovarian 100): an open-label, randomised, phase 3 trial. LANCET ONCOLOGY 10/2021

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BACKGROUND

Although most patients with epithelial ovarian cancer respond to frontline platinum-based chemotherapy, around 70% will relapse within 3 years. The phase 3 JAVELIN Ovarian 100 trial compared avelumab (anti-PD-L1 monoclonal antibody) in combination with chemotherapy followed by avelumab maintenance, or chemotherapy followed by avelumab maintenance, versus chemotherapy alone in patients with treatment-naive epithelial ovarian cancer.

METHODS

JAVELIN Ovarian 100 was a global, open-label, three-arm, parallel, randomised, phase 3 trial run at 159 hospitals and cancer treatment centres in 25 countries. Eligible women were aged 18 years and older with stage III–IV epithelial ovarian, fallopian tube, or peritoneal cancer (following debulking surgery, or candidates for neoadjuvant

chemotherapy), and had an Eastern Cooperative Oncology Group performance status of 0 or 1. Patients were randomly assigned (1:1:1) via interactive response technology to receive chemotherapy (six cycles; carboplatin dosed at an area under the serum-concentration-time curve of 5 or 6 intravenously every 3 weeks plus paclitaxel 175 mg/m2 every 3 weeks or 80 mg/m2 once a week [investigators' choice]) followed by avelumab maintenance (10 mg/kg intravenously every 2 weeks; avelumab maintenance group); chemotherapy plus avelumab (10 mg/kg intravenously every 3 weeks) followed by avelumab maintenance (avelumab combination group); or chemotherapy followed by observation (control group). Randomisation was in permuted blocks of size six and stratified by paclitaxel regimen and resection status. Patients and investigators were masked to assignment to the two chemotherapy groups without avelumab at the time of randomisation until completion of the chemotherapy phase. The primary endpoint was progression-free survival assessed by blinded independent central review in all randomly assigned patients (analysed by intention to treat). Safety was analysed in all patients who received at least one dose of study treatment. This trial is registered with ClinicalTrials.gov, NCT02718417. The trial was fully enrolled and terminated at interim analysis due to futility, and efficacy is no longer being assessed.

FINDINGS

Between May 19, 2016 and Jan 23, 2018, 998 patients were randomly assigned (avelumab maintenance n=332, avelumab combination n=331, and control n=335). At the planned interim analysis (data cutoff Sept 7, 2018), prespecified futility boundaries were crossed for the progression-free survival analysis, and the trial was stopped as recommended by the independent data monitoring committee and endorsed by the protocol steering committee. Median follow-up for progression-free survival for all patients was 10·8 months (IQR 7·1–14·9); 11·1 months (7·0–15·3) for the avelumab maintenance group, 11·0 months (7·4–14·5) for the avelumab combination group, and 10·2 months (6·7–14·0) for the control group. Median progression-free survival was 16·8 months (95% CI 13·5–not estimable [NE]) with avelumab maintenance, 18·1 months (14·8–NE) with avelumab combination treatment, and NE (18·2 months–NE) with control treatment. The stratified hazard ratio for progression-free survival was 1·43 (95% CI 1·05–1·95; one-sided p=0·99) with the avelumab maintenance regimen and 1·14 (0·83–1·56; one-sided p=0·79) with the avelumab combination regimen, versus control treatment. The most common grade 3–4 adverse events were anaemia (69 [21%] patients in the avelumab maintenance group, 63 [19%] in the avelumab combination group, and 53 [16%] in the control group), neutropenia (91 [28%], 99 [30%], and 88 [26%]), and neutrophil count decrease (49 [15%], 45 [14%], and 59 [18%]). Serious adverse events of any grade occurred in 92 (28%) patients in the avelumab maintenance group, 118 (36%) in the avelumab combination group, and 64 (19%) in the control group. Treatment-related deaths occurred in one (<1%) patient in the avelumab maintenance group (due to atrial fibrillation) and one (<1%) patient in the avelumab combination group (due to disease progression).

INTERPRETATION

Although no new safety signals were observed, results do not support the use of avelumab in the frontline treatment setting. Alternative treatment regimens are needed to improve outcomes in patients with advanced epithelial ovarian cancer.

8. Long-term clinical outcomes of tisagenlecleucel in patients with relapsed or refractory aggressive B-cell lymphomas (JULIET): a multicentre, open-label, single-arm, phase 2 study. LANCET ONCOLOGY 09/2021

Stephen J Schuster, Constantine S Tam, Peter Borchmann, Nina Worel, Joseph P McGuirk, Harald Holte, Edmund K Waller, Samantha Jaglowski, Michael R Bishop, Lloyd E Damon, Stephen Ronan Foley, Jason R Westin, Isabelle Fleury, P Joy Ho, Stephan Mielke, Takanori Teshima, Murali Janakiram, Jing-Mei Hsu, Koji Izutsu, Marie José Kersten, Monalisa Ghosh, Nina Wagner-Johnston, Koji Kato, Paolo Corradini, Marcela Martinez-Prieto, Xia Han, Ranjan Tiwari, Gilles Salles, Richard T Maziarz

BACKGROUND

In the primary analysis of the pivotal JULIET trial of tisagenlecleucel, an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, the best overall response rate was 52% and the complete response rate was 40% in 93 evaluable adult patients with relapsed or refractory aggressive B-cell lymphomas. We aimed to do a long-term follow-up analysis of the clinical outcomes and correlative analyses of activity and safety in the full adult cohort.

METHODS

In this multicentre, open-label, single-arm, phase 2 trial (JULIET) done at 27 treatment sites in ten countries (Australia, Austria, Canada, France, Germany, Italy, Japan, the Netherlands, Norway, and the USA), adult patients (≥18 years) with histologically confirmed relapsed or refractory large B-cell lymphomas who were ineligible for, did not consent to, or had disease progression after autologous haematopoietic stem-cell transplantation, with an Eastern Cooperative Oncology Group performance status of 0–1 at screening, were enrolled. Patients received a single intravenous infusion of tisagenlecleucel (target dose 5 × 108 viable transduced CAR T cells). The primary endpoint was overall response rate (ie, the proportion of patients with a best overall disease response of a complete response or partial response using the Lugano classification, as assessed by an independent review committee) at any time post-infusion and was analysed in all patients who received tisagenlecleucel (the full analysis set). Safety was analysed in all patients who received tisagenlecleucel. JULIET is registered with ClinialTrials.gov, NCT02445248, and is ongoing.

FINDINGS

Between July 29, 2015, and Nov 2, 2017, 167 patients were enrolled. As of Feb 20, 2020, 115 patients had received tisagenlecleucel infusion and were included in the full analysis set. At a median follow-up of 40·3 months (IQR 37·8–43·8), the overall response rate was 53·0% (95% CI 43·5–62·4; 61 of 115 patients), with 45 (39%) patients having a complete response as their best overall response. The most common grade 3–4 adverse events were anaemia (45 [39%]), decreased neutrophil count (39 [34%]), decreased white blood cell count (37 [32%]), decreased platelet count (32 [28%]), cytokine release syndrome (26 [23%]), neutropenia (23 [20%]), febrile neutropenia (19 [17%]), hypophosphataemia (15 [13%]), and thrombocytopenia (14 [12%]). The most common treatment-related serious adverse events were cytokine release syndrome (31 [27%]), febrile neutropenia (seven [6%]), pyrexia (six [5%]), pancytopenia (three [3%]), and pneumonia (three [3%]). No treatment-related deaths were reported.

INTERPRETATION

Tisagenlecleucel shows durable activity and manageable safety profiles in adult patients with relapsed or refractory aggressive B-cell lymphomas. For patients with large B-cell lymphomas that are refractory to chemoimmunotherapy or relapsing after second-line therapies, tisagenlecleucel compares favourably with respect to risk–benefit relative to conventional therapeutic approaches (eg, salvage chemotherapy).

9. Extended therapy with letrozole as adjuvant treatment of postmenopausal patients with early-stage breast cancer: a multicentre, open-label, randomised, phase 3 trial. LANCET ONCOLOGY 10/2021

Lucia Del Mastro, Mauro Mansutti, Giancarlo Bisagni, Riccardo Ponzone, Antonio Durando, Laura Amaducci, Enrico Campadelli, Francesco Cognetti, Antonio Frassoldati, Andrea Michelotti, Silvia Mura, Ylenia Urracci, Giovanni Sanna, Stefania Gori, Sabino De Placido, Ornella Garrone, Alessandra Fabi, Carla Barone, Stefano Tamberi, Claudia Bighin, Fabio Puglisi, Gabriella Moretti, Grazia Arpino, Alberto Ballestrero, Francesca Poggio, Matteo Lambertini, Filippo Montemurro, Paolo Bruzzi, Gruppo Italiano Mammella investigators

BACKGROUND

The benefit of extending aromatase inhibitor therapy beyond 5 years in the context of previous aromatase inhibitors remains controversial. We aimed to compare extended therapy with letrozole for 5 years versus the standard duration of 2–3 years of letrozole in postmenopausal patients with breast cancer who have already received 2–3 years of tamoxifen.

METHODS

This multicentre, open-label, randomised, phase 3 trial was done at 69 hospitals in Italy. Women were eligible if they were postmenopausal at the time of study entry, had stage I–III histologically proven and operable invasive hormone receptor-positive breast cancer, had received adjuvant tamoxifen therapy for at least 2 years but no longer than 3 years and 3 months, had no signs of disease recurrence, and had an Eastern Cooperative Oncology Group performance status of 2 or lower. Patients were randomly assigned (1:1) to receive 2–3 years (control group) or 5 years (extended group) of letrozole (2·5 mg orally once a day). Randomisation, with stratification by centre, with permuted blocks of size 12, was done with a centralised, interactive, internet-based system that randomly generated the treatment allocation. Participants and investigators were not masked to treatment assignment. The primary endpoint was invasive disease-free survival in the intention-to-treat population. Safety analysis was done for patients who received at least 1 month of study treatment. This trial was registered with EudraCT, 2005-001212-44, and ClinicalTrials.gov, NCT01064635.

FINDINGS

Between Aug 1, 2005, and Oct 24, 2010, 2056 patients were enrolled and randomly assigned to receive letrozole for 2–3 years (n=1030; control group) or for 5 years (n=1026; extended group). After a median follow-up of 11·7 years (IQR 9·5–13·1), disease-free survival events occurred in 262 (25·4%) of 1030 patients in the control group and 212 (20·7%) of 1026 in the extended group. 12-year disease-free survival was 62% (95% CI 57–66) in the control group and 67% (62–71) in the extended group (hazard ratio 0·78, 95% CI 0·65–0·93; p=0·0064). The most common grade 3 and 4 adverse events were arthralgia (22 [2·2%] of 983 patients in the control group vs 29 [3·0%] of 977 in the extended group) and myalgia (seven [0·7%] vs nine [0·9%]). There were three (0·3%) serious treatment-related adverse events in the control group and eight (0·8%) in the extended group. No deaths related to toxic effects were observed.

INTERPRETATION

In postmenopausal patients with breast cancer who received 2–3 years of tamoxifen, extended treatment with 5 years of letrozole resulted in a significant improvement in disease-free survival compared with the standard 2–3 years of letrozole. Sequential endocrine therapy with tamoxifen for 2–3 years followed by letrozole for 5 years should be considered as one of the optimal standard endocrine treatments for postmenopausal patients with hormone receptor-positive breast cancer.

10. Evaluation of COVID-19 Mortality and Adverse Outcomes in US Patients with or Without Cancer

Mariana Chavez-MacGregor, Xiudong Lei, Hui Zhao, Paul Scheet, Sharon H Giordano

ABSTRACT

Importance: As the COVID-19 pandemic continues, understanding the clinical outcomes of patients with cancer and COVID-19 has become critically important.

OBJECTIVE

To compare the outcomes of patients with or without cancer who were diagnosed with COVID-19 and to identify the factors associated with mortality, mechanical ventilation, intensive care unit (ICU) stay, and hospitalization.

DESIGN, SETTING, AND PARTICIPANTS

This cohort study obtained data from the Optum de-identified COVID-19 electronic health record data set. More than 500 000 US adults who were diagnosed with COVID-19 from January 1 to December 31, 2020, were analyzed.

EXPOSURES

The patient groups were (1) patients without cancer, (2) patients with no recent cancer treatment, and (3) patients with recent cancer treatment (within 3 months before COVID-19 diagnosis) consisting of radiation therapy or systemic therapy.

MAIN OUTCOMES AND MEASURES

mortality, mechanical ventilation, ICU stay, and hospitalization within 30 days of COVID-19 diagnosis were the main outcomes. Unadjusted rates and adjusted odds ratios (ORs) of adverse outcomes were presented according to exposure group.

RESULTS

A total of 507 307 patients with COVID-19 were identified (mean [SD] age, 48.4 [18.4] years; 281 165 women [55.4%]), of whom 493 020 (97.2%) did not have cancer. Among the 14 287 (2.8%) patients with cancer, 9991 (69.9%) did not receive recent treatment and 4296 (30.1%) received recent treatment. In unadjusted analyses, patients with cancer, regardless of recent treatment received, were more likely to have adverse outcomes compared with patients without cancer (eg, mortality rate: 1.6% for patients without cancer, 5.0% for patients with no recent cancer treatment, and 7.8% for patients with recent cancer treatment). After adjustment, patients with no recent cancer treatment had similar or better outcomes than patients without cancer (eg, mortality OR, 0.93 [95% CI, 0.84-1.02]; mechanical ventilation OR, 0.61 [95% CI, 0.54-0.68]). In contrast, a higher risk of death (OR, 1.74; 95% CI, 1.54-1.96), ICU stay (OR, 1.69; 95% CI, 1.54-1.87), and hospitalization (OR, 1.19; 95% CI, 1.11-1.27) was observed in patients with recent cancer treatment. Compared with patients with nonmetastatic solid tumors, those with metastatic solid tumors and hematologic malignant neoplasms had worse outcomes (eg, mortality OR, 2.36 [95% CI, 1.96-2.84]; mechanical ventilation OR, 0.87 [95% CI, 0.70-1.08]). Recent chemotherapy and chemoimmunotherapy were also associated with worse outcomes (eg, chemotherapy mortality OR, 1.84 [95% CI, 1.51-2.26]).

CONCLUSIONS AND RELEVANCE

This cohort study found that patients with recent cancer treatment and COVID-19 had a significantly higher risk of adverse outcomes, and patients with no recent cancer treatment had similar outcomes to those without cancer. The findings have risk stratification and resource use implications for patients, clinicians, and health systems.