Report from the Canadian Association of Medical Oncologists Annual Meeting

Lung cancer

PATHS TO BETTER OUTCOMES

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TRIAL SUMMARY: Nonsurgical management

Dudani S, Zhu X, Yokom DW, et al. Stage II non-small cell lung cancer (NSCLC) treated with nonsurgical approaches: a multi-institution report of outcomes. Canadian Association of Medical Oncology Annual Meeting, April 27, 2017, Toronto, Abstract 11.

IN BRIEF

Already known

- In stage II non-small cell lung cancer (NSCLC), standard management includes surgery, however, among patients who do not undergo surgery, there is no consensus about optimal treatment.

What this study showed

- Nonsurgical management with curative intent varied by centre and by population characteristics.
- Patients who underwent chemoradiotherapy had significantly longer overall survival than those who received radiation therapy alone.

Next step

- A randomized trial may be warranted in this population.

Standard management of stage II non-small cell lung cancer (NSCLC) is surgery, often followed by adjuvant chemotherapy. However, optimal nonsurgical management remains undefined. This study reviews stage II NSCLC patients treated nonsurgically with curative intent from 2002 to 2012 across 3 Canadian academic cancer centres. The authors assess factors associated with treatment choice, and the primary endpoint's overall survival (OS). The study included 58 patients, with a median age of 74 (range 50 to 91); 44% were female and 67% had a performance status 0-1. Stage II groupings were T2b-T3 N0 in 55%; N1 in 45%. The commonest reasons for inoperability were inadequate pulmonary reserve (27%) and medical comorbidities (24%).

Results: All patients received radical radiotherapy (RT) (median 60 Gy [range 48–75]): 73% received RT alone, 24% received concurrent, and 3% received sequential chemoradiotherapy (CRT). In multivariate analyses, CRT was less likely in patients ≥70 years (OR=0.28, 95% CI: 0.11, 0.70, p=0.006) and in patients with Charlson comorbidity scores >5 (OR=0.34 [0.13–0.90], p=0.03) or normal (<10x10^9/L) white blood cell counts (OR=0.26 [0.09–0.73], p=0.01). At the time of analysis, 74% had died. Median OS was 22.9 months (95% CI: 17.1, 26.6). Patients receiving CRT had significantly longer median OS than those receiving RT alone (39.1 vs 20.5 months, p=0.0019), a finding confirmed in multivariate analysis (hazard ratio [HR]=0.38, 95% CI: 0.21, 0.69; p=0.001). Nonsurgical approaches to management of stage II NSCLC were varied. Treatment with CRT was associated with significantly longer survival compared to RT alone.

TRIAL SUMMARY: Cisplatin vs carboplatin

Aquin T, Dawe D, Banerji S. The effect of cisplatin versus carboplatin on cancer outcomes for small cell lung cancer patients in Manitoba. Canadian Association of Medical Oncology Annual Meeting, April 27, 2017, Toronto, Abstract 30.

Small cell lung cancer (SCLC) is associated with high rates of mortality, and treatment involves chemotherapy. In non-small cell lung cancer (NSCLC), cisplatin results in superior response and survival compared to carboplatin, but causes more toxicity. Little research on carboplatin in SCLC exists, but available studies suggest equivalent survival. Nevertheless, oncologists continue to use cisplatin preferentially. In this study, authors used the population-based Manitoba Cancer Registry to identify SCLC cases diagnosed from 2004 to 2013 and completed a retrospective chart review for those treated with chemotherapy. Demographics, tumour response, and treatment toxicity were compared between cisplatin- and carboplatin-treated groups. Overall survival (OS) and progression-free survival (PFS) were evaluated using multivariate Cox proportional hazard methods.

Results: Of the 531 patients identified, 139 (26.2%) received carboplatin and 392 (73.8%) received cisplatin as part of first-line chemotherapy. More patients who received carboplatin had poor performance status (13.7% vs 7.4%), elevated LDH (lactate dehydrogenase; 58.3% vs 42.3%), and extensive-stage disease (69.8% vs 54.1%), all p<0.01. Unadjusted median OS was 245 vs 332 days for carboplatin and cisplatin. Multivariable adjusted analysis for OS using cisplatin patients completing treatment as the comparator showed hazard ratios (HRs) for carboplatin completers of 0.98 (0.75–1.26), cisplatin incompleters 0.998 (0.70–1.40), and carboplatin incompleters 1.53 (1.02–2.28). Analysis for PFS, again using cisplatin patients completing treatment as the comparator, revealed the following HRs: carboplatin completers 1.00 (0.77–1.30), cisplatin incompleters 0.79 (0.56–1.12), and carboplatin incompleters 1.18 (0.77–1.82). Receipt of cisplatin was associated with a higher chance of completing 4 to 6 cycles (80.9% vs 69.1% for carboplatin). However, those treated with carboplatin had significantly less neutropenia (57.6% vs 74.7%), nephrotoxicity (2.9% vs 13.5%), neurotoxicity (0.7% vs 12.0%), and nausea/vomiting (28.1% vs 42.6%) associated with treatment, all p<0.01. Carboplatin appears to be an equally effective treatment option for SCLC, facilitating equivalent survival while avoiding toxicity. Clinicians may wish to reexamine their preference for cisplatin.

IN BRIEF

Already known
- Oncologists tend to prefer cisplatin to carboplatin in SCLC, despite a dearth of research to justify the choice.
- In NSCLC, cisplatin results in superior response and survival compared to carboplatin, but causes more toxicity.

What this study showed
- Carboplatin appears to be an equally effective treatment option for SCLC, facilitating equivalent survival while avoiding toxicity.

Next step
- The preference for cisplatin in SCLC may need to be reexamined.

TRIAL SUMMARY: Corticosteroids and survival

Graham J, Musto G, Pitz M. Inhaled corticosteroid use and survival in lung cancer. Canadian Association of Medical Oncology Annual Meeting, April 27, 2017, Toronto, Abstract 34.

There is clinical and biological evidence that inhaled corticosteroid (ICS) use has a role in lung cancer prevention. This retrospective cohort study undertaken in Manitoba sought to assess the effect of ICS exposure on overall mortality in patients diagnosed with lung cancer. Using population-based datasets, all patients with lung cancer between 2004 and 2010 were identified. Information extracted included age, sex, histologic subtype, stage at diagnosis, date of diagnosis, and date of death. Exposure to ICS was defined as more than 60-day supply with no longer than a 3-month gap between prescriptions. Based on duration and timing of exposure to ICS, patients were categorized into 7 groups. Cox regression models were constructed to determine the effects of exposure on survival.

Results: A total of 5721 patients were identified. The majority were male, 65 to 79 years old, and had stage III or IV disease. Of these, 1574 (27.5%) were exposed to ICS. Compared to the unexposed, 2 groups had improved survival in multivariate analysis: those with continuous exposure starting no more than 2 years prior to diagnosis (HR 0.86, p=0.018) and those exposed within 6 months after diagnosis (HR 0.80, p=0.039). In stratified analysis, this survival advantage was limited to stage III and IV disease. Survival was significantly worse in those who were exposed, but stopped ICS pre-diagnosis (HR 1.56, p=0.0001).

IN BRIEF

Already known
- Inhaled corticosteroid (ICS) play a role in lung cancer prevention.

What this study showed
- ICS exposure in patients with lung cancer was associated with mortality. The effect depends on both the timing and duration of exposure.

Next steps
- Further investigate the use of ICS in this population.

TRIAL SUMMARY: Managing ALK+ NSCLC

Daaboul N, Nicholas G, Laurie S, Sekhon H. Single-centre experience with ALK+ non-small cell lung cancer management. A retrospective study at The Ottawa Hospital. Canadian Association of Medical Oncology Annual Meeting, April 27, 2017, Toronto, Abstract 62.

Some patients with non-small cell lung cancer (NSCLC) have anaplastic lymphoma kinase (ALK) rearrangements that respond to ALK inhibitors (ALKi). The objective of this study is to review management of these patients at The Ottawa Hospital Cancer Centre. Between 2012 and 2016, 37 patients had positive immunohistochemistry screening for ALK rearrangement and were considered as ALK+ NSCLC. Of these, 35 patients had a FISH (fluorescence in situ hybridization) confirmation test.

Median age at diagnosis was 63 years (range 36 to 90), 57% were women, 60% had a performance status of 0–1, and 84% were nonsmokers (including 57% lifelong non-smokers). Pathology was primarily adenocarcinoma (97%). Among metastatic patients (n=31) the first treatment provided was chemotherapy in 26% and ALKi in 61% (16 patients received crizotinib and 3 received ceritinib in a clinical trial); 81% received crizotinib and 37% ceritinib. At the time of the analysis, 44% deaths had occurred. Nineteen patients were treated with first line ALKi, median time to progression was 10.5 months (11 patients), with the rest still on treatment, with no evidence of disease progression after 9 months followup.

IN BRIEF

Already known

- Anaplastic lymphoma kinase (ALK) positive non-small cell lung cancer (NSCLC) has been shown to respond to ALK inhibitors (ALKi).

What this study showed

- Management of ALK-positive patients in one cancer centre was similar to what is described in the literature: the majority of patients received an ALK inhibitor as first- or second-line treatment.

Next steps

- Further analysis should assess if staining intensity on immunohistochemistry has any correlation with response to treatment.

COMMENTARY: Patient characteristics seen in daily practice are not always represented in the patient populations studied in randomized phase 3 clinical trials. Real-world data can provide some direction for clinicians in difficult cases where there is limited evidence or a variation in practice.[1] Managing lung cancer in Canada can be challenging in areas where there is a lack of consensus.[2] The 2017 Canadian Association of Medical Oncology (CAMO) Annual Meeting highlighted some of these challenges with retrospective studies conducted in cancer centres in Manitoba and Ontario.

In the area of NSCLC, Dudani et al performed a retrospective analysis of patients with stage II NSCLC who were treated nonsurgically.[3] The authors found that variation existed in the nonsurgical management of stage II lung cancer. Although all patients received radical radiotherapy (median 60 Gy), the majority of patients did not receive concurrent therapy (73% received RT alone, 3% received sequential chemoradiotherapy [CRT], while the remaining group of patients received concurrent CRT). These data also demonstrated significantly longer survival in patients who received CRT compared to RT alone. Prior evidence has reported the superiority of concurrent CRT over RT alone.[4]

Another challenging scenario for thoracic oncologists is the management of SCLC patients who are unable to receive cisplatin chemotherapy. Several decades ago, carboplatin was shown to be an acceptable substitute with lower toxicity.[5] In a retrospective study of 531 SCLC patients, Aquin et al found that patients who completed up to 4 cycles of carboplatin-based therapy had similar OS and progression-free survival (PFS) to those who received cisplatin.[6] Worse survival was only seen in patients who did not complete up to 4 cycles of carboplatin (HR 1.53 in comparison with patients who completed up to 4 cycles of cisplatin). These data illustrate the need for more research to reexamine the preference many clinicians have for cisplatin in SCLC.

ALK-positive NSCLC is found in only between 2% and 7% of patients.[7] The pivotal PROFILE-1014 study established crizotinib (an ALK and MET inhibitor) as first-line therapy for ALK-positive NSCLC.[8] Daaboul et al reported outcomes of a retrospective study conducted in ALK-positive patients in a Canadian cancer centre.[9] ALK inhibitor therapy use was shown to be similar to what is described in the literature.[10] Median time to progression on first-line ALK inhibitor was approximately 11 months.

The fourth abstract demonstrating the importance of real-world data in lung cancer patients was a retrospective study examining ICS use in 5721 lung cancer patients in Manitoba.[11] In comparison to the ICS-unexposed patients, survival was better in stage III/IV patients starting ICS prior to or immediately after diagnosis of lung cancer (HR 0.86, p=0.018 and HR 0.80, p=0.039, respectively). These results are interesting because, although the majority of our lung cancer patients also have a diagnosis of chronic obstructive pulmonary disease requiring ICS use, there is a lack of data describing the impact of ICS on survival. Future research may examine the association between ICS use and lung cancer survival in a prospective fashion.

Retrospective studies may not provide clinical direction with the same certainty as prospective studies. However, retrospective real-world data can contribute to the body of

evidence in a meaningful way for otherwise nonrepresented populations and clinical scenarios. These studies presented at the CAMO 2017 conference exemplify the importance of real-world data in reporting practice patterns, patient outcomes and toxicities that can inform future clinical trials, guideline development and drug funding decisions.

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