Lung Cancer − Metastatic

Saturday 24 September 2011, 11:15−13:55

27LBA LATE BREAKING ABSTRACT

A Phase II Study of Sorafenib in Patients with Locally Advanced And/or Metastatic (stage IIIB or IV) Non-small Cell Lung Cancer (NSCLC) with a K-Ras Mutation

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Background: In a pilot study [1] we found sorafenib to display clinical activity against patients with K-Ras positive NSCLC, sufficient for formal phase II testing.
Methods: Patients with K-Ras mutated NSCLC that progressed after at least 1 platinum containing regimen with adequate organ reserve, ECOG 0−2, who provided written informed consent according to local IRB regulations were eligible. A tumor biopsy confirming the presence of a K-Ras mutation was mandatory. Treatment consisted of sorafenib 400 mg BID until disease progression or unacceptable toxicity. Dose reductions and delays were specified per protocol in the face of CTC toxicities grade 3 and 4. Primary endpoint: Rate of No Progression (NPR) at 6 weeks. Secondary endpoints: duration of response, progression free survival (PFS), overall survival and treatment related toxicities. A 2-stage design was implemented (Simon's optimal design; p0 = 40%, p1 = 60%, alpha = 0.05, beta = 0.20) for a total number of 48 pts.
Results: 59 patients were entered between May 1st 2010 and February 18 2011. Median age was 58 (range 46−79) years, 17 Male/42 Female, ECOG PS 0/1/2 23/32/4. 57 patients started treatment. At 6 weeks 7 PR, 23 SD, 27 PD were observed; NPR 52.8%. Four patients stopped treatment before 2nd tumor assessment. They were regarded as progressive disease and censored from the PFS analysis. At time of analysis the median follow-up was 8.1 months (range 1−12 months), 36 patients had died. Median duration of treatment was 2.1 (range 0−12) months, 4 patients are still on treatment. Median duration of response was 4.9 (range 0−11) months. Median PFS was 2.6 (range 0−12) months, 8 patients were censored. Median OS 4.9 (range 0−12) months, 21 patients were censored. Dose modifications were realized in 16 patients, of whom 4 discontinued treatment. Most common adverse events were fatigue, hand-foot reaction, dyspnea, diarrhea and cough. Grade 3 skin toxicity was reported in 6 patients (10.5%), grade 3 gastrointestinal toxicity was reported in 7 patients (12.3%), grade 3−4 metabolic abnormalities was reported in 5 patients (8.8%), grade 3−4 pulmonary toxicity in 13 patients (22.8%).
Conclusion: Treatment with sorafenib has relevant clinical activity in patients with K-Ras mutational status. Further randomized study with this agent is warranted.

References

[1] E.F. Smit, et al. J. Thor. Oncol. 5, 719, 2010.

Melanoma and Skin Cancer

Saturday 24 September 2011, 11:15−13:15

28LBA LATE BREAKING ABSTRACT

Vemurafenib Improves Overall Survival Compared to Dacarbazine in Advanced BRAFV600E-mutated Melanoma: Updated Survival Results From a Phase III Randomised, Open-label, Multicentre Trial

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Background: Median overall survival (OS) for metastatic melanoma patients (pts) has consistently been 6−8 months in chemotherapy clinical trials. Vemurafenib (PLX4032/RG7204/RO5185426) is an orally administered inhibitor of oncogenic BRAF kinase for which median OS has not been reached after a median of 10 months' follow-up in 132 pts in a Phase II study (BRIM2). In a Phase I melanoma extension cohort of 32 pts, the median OS was 12.6 months and the 2-year survival rate estimate was 35%. The aim of the Phase III BRAF In Melanoma (BRIM3) trial (NCT01006980; Hoffmann-La Roche) was to determine if vemurafenib improves OS and progression-free survival (PFS) in melanoma pts with the $BRAF^{V600E}$ mutation.
Material and Methods: Pts with previously untreated, unresectable stage IIIC or IV melanoma that tested positive for $BRAF^{V600E}$ mutation by the cobas® 4800 V600 Mutation Test (Roche Molecular Systems, Inc.) were randomised (1:1) to vemurafenib (960 mg po bid) or dacarbazine (DTIC; 1000 mg/m^2 IV q3w). Randomisation was stratified by performance status, stage, LDH and region. At the planned OS interim analysis in January 2011 (50% of the 196 deaths needed for final analysis) the independent Data and Safety Monitoring Board recommended release of results due to compelling efficacy (OS hazard ratio [HR] 0.37; 95% CI 0.26–0.55; p < 0.0001) and to permit crossover from DTIC to vemurafenib. An updated analysis of OS with an additional 3 months' follow-up was performed. Survival data were censored at time of crossover for the 50 pts who had crossed over to vemurafenib after release of results.
Results: 675 pts were enrolled at 104 centres worldwide between January and December 2010. Median follow-up in this update was 6.21 months for vemurafenib (range <1–13.9) and 4.46 months for DTIC (range <1–11.7). The updated HR for OS was 0.44 (95% CI 0.33–0.59) favouring vemurafenib. Kaplan–Meier (KM) estimate of median OS has not been reached in the vemurafenib group (95% CI 9.59−NR) and was 7.89 months (95% CI 7.26–9.63) with DTIC. KM estimate of 6-month survival was 83% for vemurafenib and 63% for DTIC. The safety profile in vemurafenib-treated pts was consistent with that reported in previous studies.
Conclusions: In this updated OS analysis of the BRIM3 trial in pts with previously untreated $BRAF^{V600E}$-mutated metastatic melanoma, vemurafenib was associated with continued improvement in OS. Median OS after 6.2 months' follow-up has not been reached.

Nursing − Supportive Care

Monday 26 September 2011, 09:00−11:15

29LBA LATE BREAKING ABSTRACT

Unrecognised and Underprepared: an Exploratory Mixed Method Study of Informal Carers' Experiences of Supporting Someone Through Chemotherapy

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Background: Patients having chemotherapy in outpatient settings assume responsibility for monitoring and managing side effects at home. They are supported by informal carers (relatives/friends). Informal carers are important for patients' safety and wellbeing during chemotherapy, yet little is known about their needs for information and support. This study investigated informal carers' needs and experiences whilst supporting patients through chemotherapy.
Materials and Methods: A mixed methods study design was used. Data were gathered by self-completion questionnaires which were analysed descriptively. These data subsequently informed semi-structured interviews conducted with a purposively selected subsample of survey respondents. Interviews were digitally recorded, transcribed and analysed using the 'Framework' approach.
Results: Forty-eight informal carers returned questionnaires (RR: 70%) − 13 of these were interviewed. Informal carers reported their needs were met in relation to information on chemotherapy and its side-effects, but a large proportion had unmet needs regarding financial support and their own needs as carers. Few informal carers were given information on their own, and thus had little opportunity to raise issues concerning their own needs and/or worries regarding patients' care. Further, not all carers had contact details for the chemotherapy service.
Informal carers adopted 4 roles in support of patients: 'advocate', 'protector', 'symptom monitor' and 'assertive companion'. Interaction between patients and informal carers influenced the roles carers adopted. Carers felt assertiveness was important; it enabled them to enhance patients' accurate and early reporting of concerning symptoms, communicate effectively with health professionals and contribute to decision-making regarding patients' care. Not all carers felt sufficiently empowered to be assertive.
Conclusion: Informal carers are important for patient safety during chemotherapy. However, their contribution in the chemotherapy setting is generally not recognised formally by health professionals and some carers appear ill-prepared to undertake the roles they adopt during patients' treatment. Lack of preparation for, and clarity regarding, their caring role and high unmet need for support can impact negatively on carers and the support they provide patients. Research is needed to develop interventions which prepare informal carers thoroughly for their carer role. This will