9326 POSTER

Clinical presentation, pathological features and natural course of metastatic uveal melanoma (MUM) as an orphan and commonly fatal disease

L. Cerbone[1], R. Van Ginderdeuren[2], J. Van den Oord[3], S. Fieuws[4], W. Spileers[2], L. Van Eenoo[5], A. Wozniak[6], C.N. Sternberg[1], P. Schöffski[5].
[1]S. Camillo Forlanini Hospital, Medical Oncology, Roma, Italy; [2]University Hospitals Leuven, Ophtalmology, Leuven, Belgium; [3]University Hospitals Leuven, Pathology, Leuven, Belgium; [4]Catholic University Leuven, Center for Biostatistics and Bioinformatics, Leuven, Belgium; [5]University Hospitals Leuven, General Medical Oncology, Leuven, Belgium; [6]Catholic University Leuven, Laboratory of Experimental Oncology, Leuven, Belgium

Background: Uveal melanoma (UM) is a rare disease characterized by an unpredictable course and variable outcome ranging from cure by local treatment to the occurrence of untreatable metastasis. The current project is focused on the characteristics of the metastatic phenotype of the disease.
Methods: We performed data collection in 76 patients with metastatic uveal melanoma (MUM) treated in Leuven between 1957−2008. Statistical analysis involved nonparametric tests, Kaplan Meier and log rank test.
Results: The median age at diagnosis was 58 years (range 30−94). Common initial treatments were surgery (71%), brachytherapy (20%) and external beam radiotherapy (7%). 73% of primary tumor arose in choroid and 27% in ciliary body; 51% had large size, 28% medium and for 21% we have missing data. Only 19% of pts had pure spindle cell type, 49% had mixed, 15% pure epithelioid, 15% spindle with epithelioid component. Extrascleral and venous invasion were found respectively in 24% and 16% of cases.MUM was more common in women (f:m ratio 48:28). Synchronous metastases were found in only 9% of cases, all others had metachronous disease after a median interval of 40 months (range, 7−420). Statistical analysis failed to identify predisposing factors for MUM with the exception of a significant negative correlation between age at diagnosis of UM and time until metastatic disease (Spearman $p = -0.4$, $p < 0.001$). Metastasis in more than 1 organ, usually liver plus another site, was seen in 47% of cases. The most frequent metastatic site was the liver (96%), followed by lung (24%), subcutaneous (16%), bone (11%) and brain (3%) lesions. The median OS from diagnosis of UM was 47 months (range, 2−236), and only 5 months in patients with MUM (range, 1−128). 65% of MUM patients qualified for further treatment, including systemic therapy (60%), radiotherapy (7%) and surgery (7%). Systemic therapy (45 pts) included mainly chemotherapy (50%), chemotherapy plus hormones (12%), immunotherapy (3%) or hormonal therapy alone (3%). The most common drugs given were DTIC (43%), cisplatin (27%), tamoxifen (10%) or phase I agents (8%). Patient benefit (PR+SD) was seen in 16/45 patients (36%), including 2 PR.
Conclusions: In this orphan disease with female predominance metastases occur late, is mainly found but not confined to the liver, and is associated with high morbidity, as >1/3 of pts do not qualify for further therapy. Advances in MUM can only be achieved by networking of sites interested in this tumor type with systematic collection of data and tissue to improve our understanding of the molecular biology of the disease.

9327 POSTER

Ipilimumab in the common daily practice: feasibility, safety, efficacy and long-term follow-up in heavily pretreated metastatic melanoma patients

A.M. Di Giacomo[1], R. Danielli[1], L. Calabrò[1], E. Bertocci[1], C. Nannicini[1], C. Miracco[2], M. Biagioli[3], M.A. Mazzei[4], M. Altomonte[1], M. Maio[1].
[1]Clinica Ospedaliera Universitaria Le Scotte, Medical Oncology and Immunotherapy Unit, Siena, Italy; [2]Clinica Ospedaliera Universitaria Le Scotte, Pathology, Siena, Italy; [3]Clinica Ospedaliera Universitaria Le Scotte, Dermatology, Siena, Italy; [4]Clinica Ospedaliera Universitaria Le Scotte, Radiology, Siena, Italy

Background: Effective anti-tumor responses are being observed in metastatic melanoma (MM) patients (pts) treated with the anti-CTLA-4 antibody Ipilimumab in clinical trials; however, no data support the feasibility and clinical effectiveness of Ipi use in the daily practice of MM. We report on a single Institution experience utilizing Ipilimumab within a compassionate program for MM pts.
Methods: 27 stage III (2) or IV (25) pts (14 males, 13 females), median age 55 (23−77) years, ECOG performance status 0−1, with MM (23 cutaneous, 3 uveal, 1 mucosal) progressing to 3 median (1−5) systemic therapies for metastatic disease received Ipilimumab. Eight pts had evidence (6) or history (2) of brain metastases and 11 elevated (>1× upper limit of normal [ULN]) LDH values. In the induction phase (IF) pts received Ipilimumab (10 mg/kg i.v.) q3 weeks (wks) for 4 cycles; following a 12 wks rest treatment was repeated q12 wks in the maintenance phase (MF). Tumor assessment (TA) *per* modified World Health Organization Criteria was performed at baseline, week (wk) 12 (±2) and wk 24, then every 12 wks. Adverse Events (AE) and immune related AE (irAE) were collected according to Common Terminology Criteria for Adverse Events version 3.0.
Results: All pts received at least one Ipilimumab dose, and 21/27 completed the IF; the remaining 6 pts, were withdrawn for disease progression (3 pts), or AE severity (3 pts) while in PD, SD and PR. Eleven pts entered the MF. TA at wk 12 showed partial response (PR) in 1/21 or stable disease (SD) in 5/21 pts. TA at wk 24 showed PR and SD in 3/11 and 5/11 pts, respectively, with an ongoing clinical benefit (SD + PR + CR) of 30% (8/27 pts); these pts are still on treatment. Long-term follow-up of pts reaching wk 48 showed PR in 2/6 and SD 4/6 pts. The median overall survival is 29 wks (2−55). Slow, steady declines in tumor volume and appearance of new lesions with subsequent shrinking of total tumor burden has been observed. One patient experienced Grade 3 AE (myocardial infarction considered unrelated to treatment), 1 patient Grade 4 irAE (pancytopenia) and 2 pts had Grade 3 irAE (diarrhea).
Conclusions: Ipilimumab treatment is feasible, safe and clinically effective also in the common daily practice and in heavily pretreated, progressing, MM pts. A sizeable proportion of these pts experiences durable clinical benefit and long-term survival.

9328 POSTER

The Italian experience on the feasibility and safety of ipilimumab therapy in pretreated metastatic melanoma patients

M. Altomonte[1], P. Queirolo[2], A. Testori[3], P. Ascierto[4], R. Danielli[1], A.M. Di Giacomo[1], V. Chiarion Sileni[5], M. Del Vecchio[6], R. Ridolfi[7], M. Maio[8].
[1]Azienda Ospedaliera Universitaria Senese, Medical Oncology and Immunotherapy Unit, Siena, Italy; [2]National Institute for Cancer Research, Medical Oncology, Genoa, Italy; [3]European Institute of Oncology, Melanoma and Sarcoma Division, Milan, Italy; [4]Istituto Nazionale Tumori "Fondazione Pascale", Unit of Medical Oncology, Naples, Italy; [5]Istituto Oncologico Veneto-IRCCS, Medical Oncology Unit, Padua, Italy; [6]Fondazione IRCCS Istituto Nazionale dei Tumori, Medical Oncology Unit 2, Milan, Italy; [7]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Somatic Cell Therapy Unit, Meldola-Forlì, Italy; [8]Azienda Ospedaliera Universitaria Senese-Istituto Toscano Tumori, Medical Oncology and Immunotherapy Unit, Siena, Italy

Background: Clinical trials and single institution experiences have shown effective anti-tumor responses in pre-treated metastatic melanoma (MM) patients (pts) receiving the anti-CTLA-4 monoclonal antibody ipilimumab. We report the Italian (7 Institutions) experience on feasibility and safety of ipilimumab treatment of MM patients within a compassionate use program.
Materials and Methods: Seventy-two pts (43 males, 29 females), median age 57 (23−80) years, ECOG performance status 0−2, with MM (51 cutaneous, 12 uveal, 2 mucosal, 7 unknown primary), progressing to 3 median (1−5) systemic therapies for metastatic disease initiated ipilimumab treatment between February and September 2008. In the induction phase (IF) pts received ipilimumab (10 mg/Kg i.v.) q3 weeks (wks) ×4 cycles; after a 12 wks rest, upon physician judgement, pts received maintenance dosing q12 wks. First tumor assessment (TA) *per* modified World Health Organization criteria was performed at the end of the IF. Adverse Events (AE) were collected according to Common Terminology Criteria for Adverse events version 3.0.
Results: All pts received at least one ipilimumab dose, 43/72 completed the IF; the remaining 29 pts were withdrawn for early disease progression. Twenty out of 43 pts entered the MF. TA performed at the end of the IF showed partial response (PR) in 4 or stable disease in 12 pts, with a clinical benefit of 22%. Grade 3 AE were reported in 8% (6/72) pts (2 diarrhoea, 1 epigastric pain, 1 myocardial infarction, 1 tumor pain, 1 neurological event).
Conclusions: Ipilimumab treatment in heavily pretreated MM pts is feasible and safe, and results in early clinical benefit in a sizeable proportion of patients.

9329 POSTER

eNOS plays a critical role in the tumor initiation and progression in chronically stressed mice

A. Barbieri[1], G. Palma[2], A. Rosati[4], M.c. Turco[5], A. Petrillo[5], M.I. Vecchione[5], M.D.B. Di Bernardo[3], A. Giudice[5], C. Arra[5], M. Iaffaioli[5].
[1]National Cancer Institute Pascale, Experimantal Oncology, Naples, Italy; [2]Pascale, Dipartimento Di Oncolgia Sperimentale, Napoli, Italy; [3]Universita Degli Studi Di Napoli Federico Ii, Dipartimento Di Istologia, Napoli, Italy; [4]Università Di Salerno, Dipartimento Di Farmacia, Salerno, Italy; [5]Pascale, Dipartimento Di Oncologia Sperimantale, Napoli, Italy

Background: Recent studies show that the stress has an influence on immunological, neurochemical and endocrinological functions. In addition