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TSEI – Associated Malignant Melanoma in Mycosis Fungoides

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Introduction: The incidence of MM in the Israeli population according to the Annual Report for 2007 of the Israeli National Cancer Registry is 13.54 per 100,000. The risk of second primary malignancy in cutaneous T-cell lymphoma [CTCL], including non-melanoma skin cancer, has been well documented. However, reports of malignant melanoma [MM] as second primary malignancy in CTCL are rare.
Patients and Methods: The National Cancer Registry and the Rambam Health Care Campus databases were queried to identify second primary malignant melanoma in CTCL patients. As a result, a database of 200 patients was developed, encompassing the period from 1950 until June 2010.
Results: Seven mycosis fungoides [MF] cases associated with MM were identified. Five had been treated with total skin electron irradiation [TSEI], one with involved field skin electron irradiation, and one had no irradiation treatment. Two patients were treated with PUVA or MN topically and one received total body irradiation. The patients had early stages (IA-IB) of MF.
Conclusions: In CTCL patients, we found the incidence to be 7 per 199. The mechanisms of the phenomena may lay in host immunomodulation that results in CTCL pathogenesis and/or in the negative influence of electron beam treatment of susceptible persons with MF.

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Near-Infrared Guided Indocyanine Green (ICG) and Indocyanine Green With Human Serum Albumin (ICG:HAS) Sentinel Lymph Node Biopsy in Melanoma Patients

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Introduction: For a number of years now, the 'gold standard' in assessment of regional lymph node status in cutaneous melanoma has been sentinel lymph node biopsy (SLNB) using markers such as radioactive technetium and/or methylene blue. However, with the recent advent in near infrared (NIR) technology, a novel fluorophore Indocyanine Green (ICG) has been proposed as a promising alternative.
The aim of this study was to assess the usage of ICG and ICG in combination with human serum albumin (ICG: HSA) in performing SLNB of patients with cutaneous melanoma.
Material and Methods: All 10 patients with cutaneous melanoma after initial surgical resection of the tumour underwent SLNB. In five patients, ICG alone was used and the other five, a combination ICG:HSA was used. NIR PDE (Hamamatsu, Japan) camera was used to detect the lymphatic flow of ICG and ICG:HSA and to perform real time exploration. In all patients, technetium radiocolloid was used as a standard marker for SLNB.
Results: After the injection of ICG and ICG:HSA, real time lymphatic flow using PDE camera was observed in 8 out of 10 patients. In the group of patients where SLNBs were performed with ICG, total of 13 SLNs (mean 2.16) and 10 SLNs (mean 1.67) were detected with ICG and radiocolloids respectively. In the group of patients where SLNBs were performed with ICG:HSA, total of 11 SLNs (mean 1.83) and 10 (mean 1.67) were detected with ICG:HSA and radiocolloids respectively. No difference in number of lymph nodes found during biopsy between radiocolloid and fluorophores was seen $p = 0.59$.
Conclusion: SLNB with NIR guided ICG and ICG:HSA seems to be an effective alternative to radiocolloid method. Although further research is indicated for routine implementation of this method, the future holds much potential and promises.

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MIPI-TURK – Multicentric Ipilimumab Experience in Turkish Patients With Metastatic Melanoma

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Background: Ipilimumab, an anti-CTLA-4 (cytotoxic T lymphocyte-associated antigen) monoclonal antibody has been shown to enhance immune responses and induce durable clinical responses in patients with metastatic melanoma. The authors report retrospectively on metastatic melanoma patients treated under compassionate use program in Turkey among 12 centers.
Methods: Patients with metastatic melanoma were treated with ipilimumab 3 mg/kg for 4 doses on weeks 1, 4, 7, 10 as induction. Response evaluation was done on week 12. Patients with complete response (CR), partial response (PR) and stable disease (SD) at week 12 were eligible for reinduction treatment.
Results: A total of 27 patients enrolled with 23 evaluable. Ipilumumab treatment was given as 2nd, 3rd and 4th line in 21.7%, 60.9% and 17.4% of patients respectively. The numbers of patients receiving ipilimumab for 1, 2, 3 and 4 doses were 3, 2, 3, 15 respectively. Three of 23 patients were eligible for reinduction. G1/2 adverse events were reported in 43.4% of patients. G3/4 was reported in 10% of patients as skin rash and diarrhea. The most common G1/2 immune related adverse events were muscle weakness (30%) and gastrointestinal (15%). Fifteen of 23 patients completing 4 doses of ipilimumab treatment were available for response evaluation. There was no CR. The overall response rate was 40% (6/15): total of PR: 13.3% (2/15) and SD 26.7% (4/15). Median time to progression was 3.2 months (95% CI: 2.4−3.9 months). Median overall survival was not reached with 59.8% of patients are surviving within 12 months of follow up period.
Conclusions: Ipilimumab treatment is safe and effective for metastatic melanoma patients with tolerable immune related adverse events according to the accessible data so far.

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Phase 3 Randomized Study of Ipilimumab (IPI) Plus Dacarbazine (DTIC) Vs DTIC Alone as First Line Treatment in Patients With Unresectable Stage III or IV Melanoma

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Background: IPI monotherapy (3 mg/kg) improved overall survival (OS) in a phase 3 study of previously treated, unresectable or metastatic melanoma patients (pts). Current study evaluates DTIC, a global standard of care, plus IPI in first line metastatic melanoma.
Material and Methods: In this double-blind phase 3 study, pts with metastatic melanoma, ECOG PS 0/1, and no prior therapy for advanced disease, were randomized 1:1 to IPI (10 mg/kg) + DTIC (850 mg/m^2) or placebo + DTIC (850 mg/m^2) at Wks 1, 4, 7, 10 followed by DTIC q3 wks through Wk 22 (induction). Eligible pts received IPI or placebo q12 wks as maintenance. Primary endpoint was OS; 2-sided log-rank test was performed, stratified by M stage and ECOG PS at randomization.
Results: Of 502 (IPI + DTIC=250; DTIC alone=252) pts, 60% were male, 68% were <65 yrs; 71% had ECOG PS 0, 56% had M1c disease, 40% had elevated lactate dehydrogenase (LDH), and 26% received adjuvant therapy. 37% in IPI + DTIC and 65% in DTIC alone arms received 4 induction doses. A significant improvement in OS [11.2 vs 9.1 mo; HR = 0.72; P = 0.0009] with higher estimated survival rates at 1 yr (47.3 vs 36.3%), 2 yr (28.5 vs 17.9%) and 3 yr (20.8 vs 12.2%) were seen in IPI + DTIC vs DTIC alone. OS results were consistent with primary endpoint for subgroups of ECOG-PS, LDH and M stage. In IPI+DTIC vs DTIC alone arms, median progression-free survival (first assessed at ~3 mo) was 2.8 vs 2.6 mo (HR = 0.76; P = 0.006); best overall response rate was 15.2% vs 10.3%; and median response duration was 19.3 vs 8.1 mo. Grade 3/4 adverse events (AEs, regardless of attribution) were noted in 56% in IPI +DTIC (n = 247) and 27% pts in DTIC alone (n = 251) arms, including: elevated ALT (22% vs 1%); diarrhea (4% vs 0%); rash (1% vs 0%). There were no drug-related deaths in IPI + DTIC and 1 due to gastrointestinal (GI) hemorrhage in DTIC alone arm.
Conclusions: A significant improvement in OS was seen in first line metastatic melanoma pts with IPI (10 mg/kg) + DTIC vs DTIC alone and was consistent across the subgroups of ECOG-PS, LDH and M stage. Durable survival and objective responses were noted in some pts after follow-up for up to 4 yrs. Types of AEs were generally consistent with prior IPI studies; however, frequencies of some AEs differed in this study with higher transaminitis and lower diarrhea/colitis/GI perforation rates