need for the development of novel efficacious therapies. As melanoma is a highly therapy-refractory tumor, it demands effective therapeutic combinations. Suicide gene therapy has been proposed as a strategy for the treatment of intractable cancers and has been assayed in some clinical trials alone or in combination with other therapies. In this context, the *E* gene is another potentially interesting bacteriophage lysis gene for cancer therapy. In contrast to most double-stranded DNA phages, which generally encode two genes that elicit host cell lysis (endolysin and holing protein), the small single-stranded DNA phage fX174 has only one lysis gene.
Methods: To evaluate whether this *E* gene has a cytotoxic impact on melanoma cells *in vitro* and *in vivo* we selected the B16-F10 murine melanoma cell line as a model. We used a nonviral gene delivery approach (pcDNA3.1/E plasmid) to study the inhibition of melanoma cells' proliferation *in vitro* and direct intratumoral injection of pcDNA3.1/E complexed with jetPEI to deliver *E* cDNA to rapidly growing murine melanomas. The effect and mechanism action of the E protein in vitro and in vivo was studied by applying several viability (MTT), apoptosis and imagen diagnostics assays.
Results: We found that the *E* gene has both a strong antiproliferative effect in B16-F10 cells *in vitro* and induces an efficient decrease in melanoma tumor volume *in vivo* (90% in 15 days). Interestingly, the GFP-E fusion protein expressed in melanoma cells was located in the mitochondria. *In vitro* and *in vivo* analysis demonstrated significant functional and morphological mitochondrial alterations accompanied by a significant increase of cytochrome c and active caspase-3 and -9 in transfected cells, which suggests that tumoral cell death is mediated by the mitochondrial apoptotic pathway.
Conclusion: In summary, we have reported, for the first time, the ability of the *E gene* to induce the death of melanoma cells *in vitro* and *in vivo.* The successful use of this gene as a new anticancer gene therapy system may establish a role for it in cancer treatment.

9311 POSTER

MRI versus FDG-PET scan in patients with liver metastases from uveal melanoma: a prospective study with intraoperative confirmation

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Background: Resection of liver metastases is proposed to treat liver metastases of uveal melanoma (UM); microscopically complete (R0) resection of metastases improves median survival from 22 versus 9 months if incomplete surgery. The aim of this study was to compare the sensitivity of dynamic-enhanced MRI with FDG-PET in the pre-operative diagnosis of liver metastases UM.
Matherial and Methods: 15 consecutive patients (mean age 56 years (range 38−71)) underwent FDG-PET scan and liver MRI. All patients had suspected liver metastases following screening by hepatic US and/or CT scan. Extrahepatic metastatic disease was excluded by whole body CT scan and bone scintigraphy. MRI and FDG-PET were performed a mean of 19 days before surgery. Imaging findings were compared with surgical and histological findings on a lesional basis.
Results: 28 lesions were resected with 27 metastases being histologically proven. There were 9 (33.3%) lesions 10 mm. Sensitivity and positive predictive value were 66.7% and 94.7% for MRI compared to 40.7% and 100% on FDG-PET. The difference between the two methods was statisticaly significant ($p = 0.01$; Mac Nemar test). In the remaining 3 patients, diffuse miliary disease (>10 capsular lesions) was discovered intra-operatively, 2 of which had been suspected on pre-operative MRI.
Conclusions: In this study, MRI is superior to FDG-PET for the detection of hepatic metastasis of UM. Whilst in some cases miliary disease was suggested by MRI, preoperative confirmation remains imperfect so, when miliary disease is suspected, laparoscopy exploration prior to formal surgery is recommended.

9312 POSTER

Antitumor responses to ipilimumab in advanced melanoma are not affected by systemic corticosteroids used to manage immune-related adverse events (irAEs)

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Background: The monoclonal antibody ipilimumab overcomes peripheral immune tolerance by blocking cytotoxic T-lymphocyte antigen-4. The irAEs associated with ipilimumab primarily affect the skin, gastrointestinal (GI) tract, liver, and endocrine systems. Specific treatment guidelines to manage irAEs were incorporated into protocols within the ipilimumab clinical trial program for advanced melanoma, which include the use of high-dose steroids for grade 3−4 diarrhea/colitis to reduce the incidence of life-threatening complications, e.g. GI perforation. The current analyses were undertaken to determine if steroids affect ipilimumab antitumor responses.
Methods: A total of 283 advanced melanoma patients (pts) were treated in the Phase II studies CA184008, 022, and 007 with ipilimumab administered at 10 mg/kg every 3 weeks (Q3W) $\times 4$ (induction); eligible pts could continue to receive maintenance ipilimumab Q12W from Week 24. Tumor assessments were first carried out at Week 12 (end of induction period). Response was evaluated using modified World Health Organization (mWHO) criteria and novel immune-related response criteria (irRC). [1]
Results: Of 283 pts, 119 received steroids for the treatment of irAEs (Table). Eighty-three pts (29.3%) achieved disease control (DC) by mWHO criteria [complete/partial response (CR/PR), or stable disease (SD) $\geqslant$12 weeks], for which 43 received steroids. Fifteen of the 43 pts achieved CR or PR (2 pts received steroids after response only; 1 pt received steroids prior to response only; 12 pts received steroids before and after response). Of the 43 pts, 25 (58.1%) maintained DC wheres 26 of 40 (65.0%) who did not receive steroids maintained DC. Similar results were obtained using irRC.

	Achieved DC		Maintained DC		Progressive disease (PD)/Lost DC
	CR/PR	SD	CR/PR	SD	
mWHO criteria					
Steroid use (n = 119)	15	28	12	13	94
No steroid use (n = 164)	11	29	8	18	138
irR criteria (irRC)					
Steroid use (n = 119)	16	36	12	23	84
No steroid use (n = 164)	16	35	13	21	30

Conclusions: When the severity of irAEs requires steroids, there is no evidence that their use precludes the development of an antitumor response to ipilimumab, or adversely affects responses once achieved.

References

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9313 POSTER

NEMO-binding domain peptide induces apoptosis in human melanoma cells: an effect associated to inhibition of constitutive NF-kappaB activation

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Background: melanoma is the most aggressive form of skin cancer. Recent studies have identified key signalling pathways important in promoting melanoma tumorigenesis. One such important target is the Nuclear Factor-κB (NF-κB) pathway. *In vitro* studies have shown that IKK is constitutively active in human melanoma cells as compared to