043 Mechanism of action of propranolol in infantile hemangiomata: New insights from a xenograft model
F Marsin1, C Eyerich2, P Paukalanen-Checkmodine1, S Prey1, P Dulkoorg1, T Coufignal1, H Rezvani1 and A Taieb1 1 Dermatology, Bordeaux University, Bordeaux, France and 2 Cardioiology, INSERM U1013, Pessac, France

8 years after propranolol was found efficacious in infantile hemangiomata (IH), therapeutic mechanisms remain elusive. It has been shown, in an ovarian cancer model, that ADRB2 signaling is key for chronic stress induced tumor growth. In this model, tumor promotion is abolished by propranolol or ADRB2 siRNA but not by ADRB1 siRNA. In IH patients, after oral administration of 3 mg/kg/day of propranolol, plasma Cmax is below 1 pg/ml, whereas propranolol has been used in vitro at 100 μM and up to 50 mg/kg in mouse models. Thus, an animal model which recapitulates propranolol response at clinical doses is still needed. We have chosen to do an in vivo human model of xenografted malignant tumor (glioblastoma) which is very angiogenic and selectively ADRB2 positive. In such a model tumor hypoxia can be induced by the anti-VEGF-A heavyczumab (Avastin). In our model, 2 mg/kg/ day of propranolol, or ADRB2 knockdown, induces a modest inhibition of tumor induction but has no effect on doubling time. The gain in antitumoral effects is only marginal. Upon propranolol doses ranging from 2 to 50 mg/kg we observed an inverse dose response which has been already shown for periodontal disease. Elevated HIF1α in IH suggested strongly that a hypoxic environment can explain the specific response of IH to propranolol. Indeed, in the context of relative hypoxia induced by Avastin, our tumor model responds with markers shared by IH such as HIF1α, GLUT1 or MMP9. In that situation, ADRB2 knockdown as well as low dose propranolol show a significant inhibition of tumor growth. Furthermore, we could show that both propranolol and ADRB2 knockdown mediate an attenuation of MMP9 expression. Interestingly CREBL1, which is a CAMP dependent transcription factor known for binding MMP9 promoter, was also downregulated both by propranolol and ADRB2 knockdown. Moreover, potential genetic associations of propranolol antitumoral response also involved in the specific therapeutic response first evidenced in IH.

044 Cellular mechanism of action of IgE-specific immunoadsorption in treatment of patients with severe atopic eczema
F Marsin1, C Eyerich2, S Puchsch1, A Zink1, J Thomas1, T Biedermann1 and C Schmidt-Weber1 1 Hemiholz Center, ZAUM Center for Allergy and Environment, Munich, Germany and 2 Department of Dermatology and Allergy, Technical University of Munich, Munich, Germany

IgE-specific immunoadsorption (IA) is an effective treatment for severe forms of atopic eczema (AE). However, mechanisms behind this therapeutic approach and biomarkers predicting the therapeutic outcome are not yet known. This study is aimed at detecting the impact of IA on cellular level and clinical outcome. Six patients with severe AD (SCORAD>40) and highly elevated IgE levels (IgE>2.000IU/ml) were included in the study. Every patient received a total of ten IgE-specific IA sessions that were conducted in three intervals with a break of two weeks between each interval. A follow-up examination was performed four weeks after the last session. Frequencies of different immune cell populations and their receptor expression profiles as well as changes in basophil activation were monitored by flow cytometry at the beginning and the end of the first interval to detect short-term effects and at the end of the last interval, respectively, to examine medium-term effects. Finally, the follow-up analysis monitored potential long-term effects. As expected, IA decreased IgE levels, which tended to increase again overnight but showed a slight overall reduction by 11.4% at follow-up. Despite this marginal and short-term effect on serum IgE levels, IA was clinically effective with an average reduction of the SCORAD of 46.2%. At cellular level, the relative number of neutrophil granulocytes decreased over time by 34.4%, while the number of other immune cells was unaltered. Even though the frequency of FcεRIa on basophil granulocytes remained unchanged, the MFI declined. Moreover, the expression of CD32 on B cells decreased. In conclusion, although reduction of IgE levels by IgE-specific IA is not persistent, the improvement of SCORAD and patient well-being is long-lasting. Even though the underlying mechanisms are not yet fully elucidated, effects of IA at the cellular level might contribute to the clinical efficacy.

045 Psoriasis and addictions: a neglected challenge
A Zink, M Herrmann, T Fischer, A Böhrer, F Lauffer, N Garzor-Stark, T Biedermann and K Eyerich 1Department of Dermatology and Allergy, Technical University of Munich, Munich, Germany

Psoriasis affects up to 4% of the general population with an enormous socio-economic impact. Within the last few years substantial achievements have been made in understanding the pathogenesis of psoriasis, which led to the approval of a number of highly effective drugs. However, only a proportion of psoriasis patients currently receive required medical treatment. To investigate the association of psoriasis and addictions and its possible negative impact on treatment compliance, we screened psoriasis patients for the most common addictions in the general population addictions were significantly higher for alcohol abuse (p<0.0001), drug abuse, 4% at risk for food dependency and 19% compulsive gamblers. Compared to the screening tools. Thereof, 41% were regular smokers, 24% high risk drinkers, 11% at risk for food. The results were then compared to the federal report on prevalence of addictions in Germany in 2015. Of 102 patients, 57 showed addictive behaviour measured with the used screening tools. Thereof, 41% were regular smokers, 24% high risk drinkers, 11% at risk for drug abuse, 4% at risk for food dependency and 19% compulsive gamblers. Compared to the general population additions were significantly higher for alcohol abuse (p<0.005), nicotine (p<0.00005) and gambling (p<0.0001). In addition the body mass index was increased in the study population (p<0.0001). Screening measures for addictions have to be promoted for the assessment of psoriasis and can be recommended for all doctors treating patients with psoriasis. Addictions negatively affect treatment compliance and might contribute to the undertreatment of patients with psoriasis in general. Parallel to new drug approvals and even more detailed insights into pathomechanisms of psoriasis, public health strategies and interdisciplinary approaches are essential for the future of sustained psoriasis healthcare.

046 Epidemiology of lentigo maligna and lentigo maligna melanoma in the Netherlands, 1989 – 2013
K Greveling1, M Wijkker, T Nijsten, RR van den Bos2 and L Hollstein Dermatology, Erasmus MC Cancer Institute, Rotterdam, Netherlands

Lentigo maligna (LM) is considered a precursor to LM melanoma (LMM). We assessed trends in LM and LMM incidence rates between 1989 and 2013, in the Netherlands, and estimated the risk of a LMM after LM. Data on newly diagnosed LM and LMM were obtained from the Netherlands Cancer Registry and PALGA (Dutch Pathology Database). Age-standardized incidence rates (European standardized rate [ESR]), estimated annual percentage changes (EAPC), and the cumulative incidence of LMM after LM were calculated. Between 1989-2013, 10,545 patients were diagnosed with a primary LM and 2,898 with a primary LMM in the Netherlands. The ESR for LM increased from 0.72 to 1.84 per 100,000 person-years, and for LMM from 0.24 to 1.91 between 1989-2013. LM incidence increased from 2002-2013 (4.8% annually) to 2005-2013 (~20% per year) — rise in LM incidence from 2007-2013 (EAPC 12.4%). The cumulative incidence of LMM after a primary LM after 25 years follow-up was 2.0% for males and 2.6% for females. The increased incidence of LM and LMM in the Netherlands seems, besides increased awareness, increased histological confirmation, diagnostic drift and changed market forces, to reflect a true increase. The absolute risk of a LMM (at any location) after a histologically confirmed LM was low (2.0 – 2.6%).

047 Validation of the Self-Assessment Vitiligo Extent Score (SA-VES) as a patient reported outcome
N van Geel1, J Lommerts1, M Bekkenko1, CA Prinsen2, V Ellefesadou3, A Taieb1, M Picard1, K Erzéline4, A Wolkerstorfer5 and R Speeckaert1 1Dermatology, Erasmus MC Cancer Institute, Rotterdam, Netherlands, 2Dermatology, Erasmus MC, Rotterdam, Netherlands, 3Centre of Evidence Based Dermatology, University of Nottingham, Nottingham, United Kingdom

The Vitiligo Extent Score (VES) has been introduced recently for the clinical assessment of vitiligo extent. We developed a simplified version of this structured instrument as a self-administered tool (SA-VES) for patients. Patients were asked to fill in the scoring template and were invited to complete this again after 2 weeks. In addition, clinical pictures of vitiligo patients were obtained by 2 dermatologists using the patient reported version of the VES. Ninety-two patients completed the form twice. The SA-VES demonstrated a very good intra-rater reliability (intraclass correlation for BSA = 0.868 (95% CI: 0.693-0.947)). According to the patients this evaluation method was easy and easy to understand, 71% (95% CI:0.708-0.963). The results of this study support the general validity of the SA-VES and demonstrate that the SA-VES is a good tool for the assessment of vitiligo. This patient oriented evaluation method may be useful in daily practice and epidemiological studies.

048 Prevalence of skin diseases in hospitalised geriatric patients - a pilot study
E Makranzani1, E Steinhagen-Thiessen1, R Nierzaj2, C Zouboulis1 and R Eckardt1 1Department of Dermatology and Allergic Diseases, Universitätsklinikum Ulm, Ulm, Germany, 2 Research Group on Geriatrics, Charité Universitätsmedizin Berlin, Berlin, Germany and 3 Department of Dermatology, Venerology, Allergology and Immunology, Städtisches Klinikum Dessau, Berlin, Germany

Information regarding the skin health status of geriatric patients still remains sparse. The goal of our study was to investigate the extent of dermatological diseases in hospitalised elderly patients, map the most prevalent ones, check for any gender differences and document any correlations with duration of hospitalisation and results of geriatric assessments. 110 hospitalised geriatric patients underwent a complete dermatological examination in the Geriatric Hospital ‘Evangelisches Geriatriezentrum Berlin’. The collected information was structured according to dermatological diagnosis, results of geriatric assessments, duration of hospitalisation, age and gender of the patients. The average number of diagnosed skin diseases per patient was for the female population 3.7 ± 1.8 and the male population 4.3 ± 1.8. After categorising all diagnosed skin diseases infectious diseases showed to be most common both in females and males (55% and 58%, respectively) followed by vascular diseases (46.7% and 54 %, respectively). Precancerosis skin lesions and epithelial skin cancer were more frequent in men than in women (20% vs. 6.7%, p=0.037 and 34% vs. 13.3%, p<0.010, accordingly). Pruritus correlated positively with the duration of hospitalisation and negatively with Barthel-Index and Tinetti-Score on the day of discharge, indicating that pruritus may have significant impact on the physical condition of elderly, multimorbid patients. Our results show that skin health in the elderly is compromised and disregarded and this should constitute one of the top priorities of health care specialists and physicians in the future. The aged population and especially men need closer monitoring because of lack of compliance and physical limitations.