Poster Board 1

**Proof of Feasibility and Efficiency of a Novel Polarimetric Dermatoscope for the Diagnosis of Skin Cancer**

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**Background**

The ratio of excisions of benign to malignant lesions for suspected malignancy remains very high. This results in unnecessary excisions causing unjustified scars and morbidity, and heavy costs on health care systems. We have developed a new device – a polarimetric dermatoscope measuring differential polarization to discover the nature of skin lesions.

**Objective**

To perform an initial "proof of concept" (POC) study to check whether the device can differentiate benign and malignant skin lesions with a high level of accuracy.

**Patients & methods**

139 pigmented skin lesions of 63 patients were examined. The lesions were photographed clinically and dermoscopically and scanned by the research device. Seventy seven lesions were surgically removed and subjected for histological examination. The clinical and dermoscopic photographs of the lesions were examined by experienced blinded dermoscopists and each of the lesions was assigned a suspicion level for being malignant. Research device scans were graded on a scale of 1-10 where 1 is completely benign and 10 is highly suspicious for malignancy. The correlation between the device results and the clinical and dermoscopic predictions was compared to the histology results considered "gold standard" and to each other. The correlation was measured as specificity and sensitivity and by Pearson coefficient as a measure for inclusive correlation.

**Results**

The correlation between the device’s and histological results resulted in a sensitivity of 1.0 and specificity of 0.9167 resulting in a Pearson coefficient of 0.645. As a comparison the correlation between the clinical and histological and dermoscopy and histology resulted in a sensitivity of 1.0 and 0.75 and specificity of 0.32 and 0.89 resulting in a Pearson coefficient of 0.172 and 0.447 respectively.

**Conclusions**

Despite the relatively low number of lesions examined the research results indicate a significantly higher sensitivity and specificity of the device as compared to both the clinical and the dermoscopic evaluation.
The Novel Role of 11β-Hydroxysteroid Dehydrogenase 2 in Non-Melanoma Skin Cancer Development and Progression

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Background

11β-hydroxysteroid dehydrogenase type 2 (11βHSD2) deactivates cortisol to cortisone. It is up-regulated in non-melanoma skin cancer (NMSC) cells. We found that glycyrrhetinic acid (GA)-mediated inhibition of 11βHSD2 protein caused a significant reduction in tumor number, weight, incidence, and significant delay in tumor onset. In addition to the use of specific inhibitors such as GA to sustain the bioavailability of glucocorticoids (GC), modifying the structure of GC molecule to prevent inactivation by 11βHSD2 is an additional way to control the action of 11βHSD2.

Objective

To test the hypothesis that modification of the functional group of cortisol at the C-11 position to a fluorine (to create 11-doxyfluorocortisol; FMOD) would increase efficacy of proliferation inhibition.

Methods

A panel of normal human epidermal skin cells (HaCaT), and skin cancer cells (PM-1; pre-cancer and Met-4; metastatic NMSC) were used. Western blot analysis to measure enzyme levels. MTT assay to measure viability of treated cell lines and qPCR to determine expression of inflammatory markers.

Results

Our results show that 11βHSD2 expression is increased in human NMSC cells vs. the normal cells. HaCaT cells were more sensitive to GC treatment compared with cancerous PM1 and Met4 cells, and the potency of FMOD against cell proliferation is at least as powerful as original cortisol if not stronger. Preliminary data showed that the LPS-induced increase of inflammatory cytokine IL-1β was significantly suppressed to a similar extent by cortisol and FMOD.

Conclusion

Modifying the structure of GC to circumvent the metabolic effect of 11βHSD2 enzymes is a novel therapy model. Further, the use of FMOD to treat inflammation and cancer, as well as prevent GC-resistance is an important area of translation research.
Matrix Metalloproteinases MMP1, MMP-2 and MMP-13 are Overexpressed in Primary Nodular Melanoma

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Background

Nodular melanoma (NM) has a tendency to show an early distant metastasis to vital organs. The invasion and spread of malignant cells involves reorganization and degradation of the extracellular matrix using several proteolytic enzymes including matrix metalloproteinases (MMPs).

Objective

The aim of this study was to investigate the expression of MMP-1, MMP-2 and MMP-13 proteins in primary nodular melanoma and dysplastic nevi to obtain a more comprehensive understanding of the MMPs function, its correlation to invasion, BRAF V600 mutation status and overall survival.

Methods and Results

Our study groups were patients diagnosed with vertical growth phase melanoma of nodular type (NM) (n =52) in the period from 2007 to 2011, and patients diagnosed with dysplastic nevi (n=28) from 2010 to 2015. After TMA construction and immunohistochemical staining, the MMPs protein expression was assessed by scoring the intensity of the staining. The results demonstrated statistically significant level of all MMPs in tumor samples compared to dysplastic nevi (p<0.001). This study revealed an interesting finding that MMP1 and MMP 13 protein expression in the BRAF V600 mutated melanoma were significantly lower than in the BRAF V600 wild type ( p<0.05). Unlike previous studies performed on mouse models or melanoma cell culture which have reported that BRAF V600 mutation activates MMP-1 expression, we could not find this connection.

Conclusion

Cox proportional hazard analysis for predictors of overall survival in the group of 52 NM patients revealed that Clark categories and MMP1 protein expression are prognostic factors for the overall survival ( p<0.05): (HR=5.97, 95% CI: 1.26-28.22 and HR=1.93; 95% CI: 1.00-3.74, respectively).
Multimodal Optical Imaging for NMSCs Detection and Therapy Guidance: A Clinical Study

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The increasing incidence and prevalence of NMSCs, especially in an increasingly older population, combined with increasing Mohs surgery costs has led to the search for new and more efficient diagnostic imaging and therapy guidance approaches. However, proper selection of the therapy method and successful therapy requires precise delineation of skin cancer margins, which is not possible with ultrasound or MR imaging due to their limited resolution. To address this problem, reflectance confocal microscopy (RCM) and optical coherence tomography (OCT) were combined within the same instrument to achieve comprehensive 3-dimensional skin imaging in vivo (see imaging capabilities in Fig. 1). In a clinical study on 85 patients, with either clinically-suspicious (n=60, in intact skin) or biopsy-proven BCCs (n=25, in scarred skin) we correlated BCC features in RCM and OCT images with histopathology, calculated diagnostic accuracy and correlated depth predicted by OCT with histopathologically measured depth. The main features were small tumors extending from the basal cell layer at the dermal-epidermal junction; small and large tumor nests; in dermis; dark silhouettes; dilated blood vessels; horn cyst and bright peritumoral stroma. Deeper features such as necrosis and intratumoral mucin pools were correlated on OCT and histology. Higher sensitivity and negative predictive value (100%) and comparable specificity (48% vs 56% on RCM) and positive predictive value (82.19 vs 84.59 % on RCM) were observed for the combined RCM-OCT device for diagnosis of all lesions (n=85). Relatively higher specificity (94.1%) and positive predictive value (75%) were observed in the clinically suspicious lesions (n=60, in intact skin). High correlation was observed (R=0.86) between the OCT predicted depth and histopathologically measured depth. Therefore, RCM-OCT imaging may be prospectively used to comprehensively diagnose suspicious BCC lesions, determine subtype and triage for treatment.

Fig. 1. Example of CM-OCT combined use for delineating BCC images: A) Clinical image showing an exophytic mass on the right shoulder. B) Dermoscopy image showing uniform white lines and serpentiform vessels, suggestive of superficial basal cell carcinoma. C) Cross-sectional and D) E) En-face OCT images showing multiple hyperdense areas, suggestive of basal cell carcinoma. D) Reflectance confocal microscopy showing core-like structure with palisading (arrow) surrounded by stratified collagen and inflammatory cells. E) Histology showing superficial tumor nests (arrows). (Hematoxylin & eosin, 4x magnification).
In Vitro Study of Sonodynamic and Photodynamic Therapy on G361 Human Melanoma Cell Line.

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Background
Sonodynamic therapy is the use of an agent that is sensitive to ultrasound, allowing deeper penetration and destroying of abnormal cells. Ultrasound-induced cytotoxicity of sonochemical sensitizers inhibits tumor growth. Photodynamic therapy is a treatment modality of tumours. The photochemical interactions of sensitizer, light, and molecular oxygen produce singlet oxygen and other forms of active oxygen, such as peroxide, hydroxyl radical and superoxid ion. The resulting damage to organelles within malignant cells leads to tumor ablation.

Objective
In this study disulfonated chloroaluminum phthalocyanine was selected for testing as a potential sensitizer for combination of sonodynamic and photodynamic therapy. We report the production of reactive oxygen species on G361 melanoma cells.

Methods
The production of ROS was investigated by molecular probe CM-H$_2$DCFDA. The light emitting diodes (LEDs 670 nm, FWHM 15 nm, 10 mW.cm$^{-2}$) were used as a source for evocation of the photodynamic effect. Ultrasound generator with transducer area 4cm$^2$, frequency 1 MHz and intensity 2 W.cm$^{-2}$ was used for evocation of sonodynamic effect. Cell damage was evaluated using fluorescence microscope microscopy.

Results
The quantitative ROS production changes in relation to sensitizer concentration, irradiation doses and ultrasound intensity were proved by fluororeader. Ultrasound treatment can support the photodynamic effect because sensitizer can be relocalized in the cells. Efficiency of photodynamic therapy and sonodynamic therapy is affected by a number of factors including absorption spectrum of the photosensitizer, wavelength of the activation light, depth of the light and ultrasound penetration in the biological tissue, tissue answer on singlet oxygen.

Conclusion
Our results indicate a synergistic effect of chloroaluminium phthalocyanine, light and ultrasound on reactive oxygen species production in G361 melanoma cells. This work was supported by the project LO1304
Electrochemotherapy in the Treatment of Locally Advanced or Recurrent Periocular Basal Cell Carcinomas

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Background
In cosmetically sensitive areas some tumors may not be amenable to simple surgical treatment. Alternatives to the surgical management may be preferred under certain circumstances. There is increasing evidence about the effectiveness of electrochemotherapy (ECT) in the treatment of basal cell carcinomas in the head and neck region.

Objective
The aim of the present study is to evaluate our results of electrochemotherapy in the treatment of locally advanced primary and recurrent eyelid-periocular basal cell carcinomas.

Methods
Thirteen patients with basal cell carcinoma involving the eyelid-periocular region were treated with ECT. All treatments were performed according to the ESOPE guidelines, using Cliniporator TM device. All patients received bleomycin based ECT. The route of administration was intratumoral in 3 patients and intravenous in 10 patients. Tumor response was evaluated using the RECIST 1.1 criteria. The median follow-up time was 12 months.

Results
Ten patients with recurrent tumors and 3 patients with primary tumors were treated. Eight patients had tumors in other extraorbital locations too. Complete response was achieved in all 13 cases in the periocular localization while in case of one patient a partial response was achieved on the nose. Lower eyelid ectropion was developed in 3 patients which had to be corrected surgically. The median follow-up time was 12 months.

Conclusion
ECT can be used effectively in the treatment of locally advanced or recurrent basal cell carcinomas in the eyelid-periocular region. Excellent tumor control can be achieved with good functional and cosmetic results without systemic side effects.
**Surgical Treatment of Neglected Malignant Melanomas of the Head and Neck Region**

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**Background**

Neglected, locally advanced head and neck melanomas represent a treatment challenge and require a multidisciplinary approach.

**Methods**

Five cases of neglected head and neck malignant melanoma were retrospectively studied which were treated in our institute between 2008 and 2018. All included patients sought medical attention only after the appearance of distressing symptoms (bleeding, disturbed vision). After the biopsy revealed malignant melanoma, wide surgical excisions of the primary tumors were performed. Reconstructive procedures were chosen on an individual basis regarding to the size of the defects, patient age and prognosis. All patients received oncologic therapies according to their stages of disease.

**Results**

Four of the tumors were developed on the cheek, two of these involving the lower eyelid, and one tumor located on the forehead and scalp. Defect size after tumor resection ranged from 45 to 310 mm in diameter. In two cases cervicofacial flap with malar bone periosteal anchoring were performed, in one case a modification of the Mustardé flap with amniotic membrane grafting, a rotation flap in combination with full thickness skin graft, and a split skin graft respectively. In the early postoperative period partial wound dehiscence were observed in two cases, and mild edema in one flap. After median follow up of 34 months (11-63 months) we achieved good aesthetic and functional result.

**Conclusion**

Neglected malignant melanomas of the head and neck region require individual multidisciplinary approach. Though in this aesthetically sensitive area the size of the lesions may seem frightful, the principles of the surgical management remain the same. However patient age, defect location, size and potential donor site should be carefully considered when planning the restoration to achieve improved aesthetic and functional outcome.
Transverse Glabellar Flap - New Method for Reconstruction after Medial Canthal Tumor Resection

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**Background**

Reconstruction methods after tumor resection in medial canthal area have been limited. Small structures including lacrimal punctume, medial canthal tendon and caruncle restrict simple approach to reconstruction and it is also hard to achieve cosmetic result in this area. The authors propose better option rather than inappropriate previous methods.

**Objective**

Previous methods mainly use forehead tissue to reconstruct defect after tumor resection in medial canthal area. However it leads to unnatural result including destroyed wrinkles on the forehead and trapdoor effect caused by difference of tissue thickness between forehead and medial canthal area. The authors have used transverse glabella flap aiming improved cosmetic results.

**Material and Methods**

After resecting tumor located in unilateral medial canthal area, transverse flap is elevated in glabella of the same size. The width of flap is 1cm, and length is 2~3cm. This flap use branch of supraoptic artery as a pedicle. After transposing flap to defect, undermining superior and inferior area of donor site should be done to close donor site defect.

**Results**

From January 2015 to December 2017, authors used 3 transverse glabella flaps to reconstruct medial canthal area defect in 3 patients. No complication including transverse scar, ectropion, telecanthus and recurrence was noted until the end of 1-year follow-up. Patients were satisfied with the result.

**Conclusion**

Medial canthal area is complex region to reconstruct after tumor resection. Transverse glabella flap using adjacent tissue from defect leads to better outcome compared with traditional methods. This method can be new and better option for reconstruct medial canthal area defect.
The Potential Use of Microneedles as an Alternative Method for Skin Cancer Treatment

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Background

Non-melanoma skin cancers (NMSC) are one of the most common cancers in humans, representing 80% of skin cancer cases each year. The majority of NMSCs (80%-90%) occur on the head and neck and surgical excision is typically the treatment of choice. However, this is often accompanied by serious side effects including changes to appearance with immense consequences on the patients’ quality of life.

One way to achieve eradication of the cancer with good cosmetic outcome may be by localized, targeted immunotherapy. Delivery, at the tumour site, of therapeutic amounts of cytokines that can trigger natural killer cells may be achieved using microneedle technologies.

Objective

To investigate whether microneedles can provide a core scientific platform from which novel, non-invasive delivery systems can be developed for the direct and localised delivery of therapeutic amounts of cytokines for immunotherapy. Tumour necrosis factor A (TNF-a) is used to investigate the proof-of-principle concept.

Methods

Rapidly dissolving microneedle devices made of carbohydrate formulations were prepared by a low vacuum deposition method, each containing 1μm of TNF-a. Skin diffusion was studied using Franz cells and porcine skin and ELISA to quantify TNF-a in the receptor phase.

Results

Initial data showed that it is possible to integrate within the microneedle formulation (consisting of carboxymethyl cellulose, maltose and trehalose) small doses of TNF-a. Diffusion studies showed enhanced distribution of TNF-a in the skin when used through the microneedle formulation compared to the control (disk without needles consisting of same sugar-TNF-a composition as microneedle array).

Conclusion

Preliminary results show that dissolving microneedles can potentially provide an enhanced non-invasive method for treating skin cancer via the localized delivery of immunotherapeutics. These can be ultimately developed into patches that patients can self-administer thus improving patient compliance and economic burden.
Melanoma and SCC Developing on the Burn Scar

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Background
Up to 2% of chronic burn scar lesions can transform into malignant tumors. Most of them are squamous cell carcinoma SCC, less basal cell carcinoma BCC. Most burn scar carcinomas are diagnosed about 30 years after the burn, and most are well-differentiated squamous cell carcinomas. The incidence of melanoma is very low.

Objective
Case report of two different and independent tumors, SCC and melanoma on burn scar

Method
We reported a case of patient with a melanoma developed on a burn scar on the back area (2009) and then after 3 years (2012) we noticed new carcinoma, squamous cell carcinoma, on the same burn scar. 67-years-old male before 53 years was accidentally injured with boiling water. 46 years after on burn scar he noticed the painless black area in the middle of the scar. We performed the wide surgical excision and local flap reconstruction.

Results
Histopathology analysis confirmed ulcerated SSM in a scar tissue (Breslow 0,85mm, Clark III, pT1b). Also lentiginous melanocytic hyperplasia (LMH) was presented. During the follow-up, after 3 years persistent area of erythema and desquamation was revealed on the lumbal area. We performed the wide surgical excision with skin auto transplantation. Histopathological analysis was consistent with intraepithelial squamous cell carcinoma with clear margins. Without dissemination of melanoma or SSC.

Conclusion
Plastic surgeons should carefully observe burn scars and performed surgical treatment of suspicious lesions. The prognosis of 5-year survival rate of melanoma in an old burn scar is not worse than that of non-burn scar carcinoma.
Altitude and Malignant Cutaneous Melanoma Risk

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Background
The risk of developing skin cancer is closely linked to exposure to ultraviolet radiation (UR). Personal and environmental factors can modulate the risk.

Objective
To analyze the incidence of invasive malignant cutaneous melanomas (MCM) in the Trento province (north east Italy, 540,000 inhabitants), according to the altimetric level, considering gender and morphology of MCM.

Methods
The incident cases recorded in the period 2009-2012 were computed according to the altimetric levels defined by the National Institute of Statistics: plain (up to 300 masl), hill (300-700), mountain (over 700). For each altitude level the average annual incidence rate has been calculated, by gender and morphology of MCM.

Results
The incident cases of MCM in the period 2009-2012 are 394, 46% males and 54% females; 98 new cases a year, with growing trends in both genders. The prevalent site (51%) in males is the trunk, in females the lower limb (38%). The analysis of the standardized 2009-2012 incidence rates stratified by altitude and morphology shows a decreasing gradient only for males and for superficial diffusion and lentigo maligna melanoma (the forms most correlated with photo exposure) with a standardized incidence rate of 11.0 /100,000 in the plains, 7.6 in the hills and 4.9 in the mountains, with a statistically significant difference between plains and hills.

Conclusion
The study indicates an inverse effect of altitude on the risk of MCM, more evident in males living in the valley bottom. Behavioral factors that result in intermittent exposure to UR could partially explain this.
MUG-Mel2, a Novel Highly Pigmented Cell Line

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Background

NRAS mutation in melanoma has been associated with aggressive tumor biology and poor prognosis. Although targeted therapy has been tested for NRAS mutated melanoma, response rates still appear much weaker, than in BRAF mutated melanoma.

Objective

While plenty of cell lines exist, however, only few melanogenic cell lines retain their in vivo characteristics. In this work we present an intensively pigmented and well-characterized cell line derived from a highly aggressive NRAS mutated cutaneous melanoma, named MUG-Mel2.

Methods

We present the clinical course, unique morphology, angiogenic properties, growth characteristics using in vivo experiments and 3D cell culture, and results of the exome gene sequencing of an intensively pigmented melanogenic cell line MUG-Mel2, derived from a cutaneous metastasis of an aggressive NRAS pQ61K mutated melanoma.

Results and Conclusion

Amongst several genetic alterations, mutations in GRIN2A, CREBP, PIK3C2G, ATM, and ATR were present. These mutations, known to reinforce DNA repair problems in melanoma, might serve as potential treatment targets. In vitro and in vivo imaging achieved an enormous contribution to the detailed characterization of the new established cell line MUG-Mel2. The aggressive and fast growing behavior in animal models and the obtained phenotype in 3D culture reveal a perfect model for research in the field of NRAS mutated melanoma.
Gender and Thickness are Important Risk Factors for Recurrence in Korean Localized Melanomas

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Background
Although predicting recurrence is important for localized melanoma, there is lack of study for investigating prognostic risk factors of recurrence in localized melanoma in Asian patients, with predominant acral melanomas.

Objectives
To find out risk factors of recurrence in localized melanoma in Asian patients.

Methods
In this retrospective study, cutaneous melanoma patients visited and followed-up for more than 6 months at the department of dermatology in Severance hospital from 2000 to 2018, without evidence of nodal or distant metastasis, were reviewed.

Results
A total of 340 patients diagnosed with cutaneous melanoma and staged as melanoma in situ, stage I or II at Severance Hospital were reviewed. Acral melanoma (239/340) was predominant. 92 patients showed recurrence after the removal of primary melanoma and included 29 local recurrences, 49 regional metastasis and 28 distant metastases. Male (p=0.030) and Breslow thickness 1mm (p=0.008) were correlated with increased risk of recurrence. Tumor mitotic rate higher than 4/10HPFs was related with higher distant metastasis (p=0.048). Breslow thickness 2.5mm in males and 4mm in females showed higher predictive value for recurrence compared to stage IIB and IIC. (RR 4.947 vs 3.689, HR 3.743 vs 2.972)

Conclusion
Sex (male) and Breslow thickness are prognostic factors for recurrence in Asian localized cutaneous melanoma and different cutoffs of thickness are predictable for male (2.5mm) and female (4mm).
Risk Factors of Recurrence and Validity of Staging Systems in Cutaneous Squamous Cell Carcinoma after Mohs Micrographic Surgery; Retrospective Review of 237 Patients

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Mohs micrographic surgery (MMS) is known to have lower recurrence rate compared to conventional wide excision for removal of cutaneous squamous cell carcinoma (cSCC). However, cSCC do recur in subsets of patients even after MMS, so predicting recurrence is important for the prognosis but studies regarding risk factors are mostly from Western countries. In this study, we aimed to analyze clinical risk factors for recurrence and investigate the role of MFN-2 as a predictive biomarker for recurrence in cSCC.

A total of 237 patients with cSCC treated by MMS were included in the study. Among them, 36 patients showed recurrence (21 patients with local recurrence and 15 patients with distant metastasis). In these patients, factors such as history of organ transplantation ($p=0.048$), comorbidity of diabetes ($p=0.026$), history of other malignant cancer ($p=0.023$) and poorly differentiated histopathology of cSCC ($p=0.024$) were correlated with recurrence. History of trauma on the cSCC site ($p=0.035$) and poor differentiation ($p=0.019$) were related with higher local recurrence. Poor differentiation ($p=0.001$) correlated with higher risk of distant metastasis. Among four staging systems, AJCC 8th staging system showed the highest predictive value. Immunohistochemical staining results showed that MFN-2 expression was higher in recurred cSCC group compared to non-recurred primary cSCC group. However, the expression level difference was not statistically significant ($p=0.188$).

In conclusion, poor differentiation histology, solid organ transplantation recipient, comorbidity of diabetes mellitus, history of other malignancy and trauma history on the site of cSCC were high-risk factors for recurrence and AJCC 8th staging system is the most predictable system for predicting recurrence in Asian cSCC patients treated by MMS. Also, our study results suggest that MFN-2 could be a candidate for predictive biomarker for cSCC, however, further studies are needed for validation.
Far From Luck’s Way: A Concurrence of Kaposi Sarcoma and Cutaneous Angiosarcoma in the Setting of Chronic Lymphocytic Leukemia

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Background
Chronic lymphocytic leukemia (CLL) is a proliferative monoclonal B-cell disorder that constitutes the most common form of leukemia in adults. The accumulation of functionally incompetent lymphocytes along with immunosuppressive treatment disrupt the immune system and lead to high incidences of secondary malignancies, among which skin cancers constitute a high incidence. Kaposi Sarcoma (KS) and cutaneous angiosarcoma are rare vascular skin malignancies encountered in the immunosuppressed population. Although synchronous angiosarcoma and KS have been documented, their coexistence with underlying CLL has not been previously reported.

Objective
Herein, we present a case of CLL, with consecutive diagnoses of KS and angiosarcoma.

Case
A 51 year-old male patient with a two-year history of CLL presented with a purple plaque located in the medial left ankle that was diagnosed as KS (Figure 1). The lesion remained stable and was followed-up without intervention. After a quiescent period of 2 months, the patient presented with exophytic vascular lesions located on his right mid-plantar region which were excised and diagnosed as Angiosarcoma (Figure 2). Further adjuvant treatment consisting of Paclitaxel and Carboplatin with consolidation radiotherapy was carried out.

Conclusion
Although rare, synchronous secondary skin malignancies can be encountered in the setting of immunosuppression. Treatment in such circumstances can pose a challenge as multiple aggressive treatment modalities may not be followed through simultaneously. In these cases, treatment should be modified to target the most aggressive tumor, followed in order of severity. Therefore local and systemic treatment was primarily focused on angiosarcoma in our patient, followed by CLL and KS.

Although angiosarcoma and KS have both been reported as secondary tumors in CLL, our case is the first reported concurrence of both malignancies in a CLL patient. Both the presentation of the malignancies and the algorithm for treatment make this case a unique contribution to the literature.