Results and discussions VAL-083-treated mice showed significantly smaller tumours compared to control (−83% for VAL-083, p<0.001) and bevacizumab (−75% for VAL-083, p<0.001). Additionally, analysis of tumour growth in time showed significantly reduced tumour progression for VAL-083 +bevacizumab compared to VAL-083 alone (p<0.01).

Conclusion These results show strong in vitro efficacy of VAL-083 alone in reducing tumour growth of an MGMT-unmethylated, recurrent GBM tumour and potentially even better for VAL-083 +bevacizumab.

PO-015 POTENTIATING ANTI-NEOPLASTIC EFFECT OF CISPLATIN BY A PROTEIN ARGinine METHYlTransferase 5 SELECTIVE INHIBITOR IN LUNG ADENOCARCINOMA CELLS

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Introduction Protein arginine methyltransferase 5 (PRMT5) is an enzyme that is greatly implicated in diverse cellular processes, including transcriptional regulation, RNA metabolism, and cell-cycle regulation. It was found in previous studies to be highly expressed in cancers including lung adenocarcinoma, Hepatocellular Carcinoma (HCC), and melanoma; in amounts much more significant as compared to benign tissues; raising evidence that PRMT5 is involved in tumorigenesis. Recent studies have proven that inhibition of PRMT5 in HCC cells through the use of AMI-1, a water soluble selective protein arginine methyltransferase inhibitor significantly reduces the proliferation and migration of HCC cells. It was also found that β-catenin is a target of PRMT5, therefore inhibiting PRMT5 resulted in the silencing of β-catenin; as well as its downstream cell-cycle regulator cyclin D1. The aim of our study is to investigate the effect of PRMT5 inhibitor (AMI-1) on the proliferation, migration and survival of lung adenocarcinoma cells.

Material and methods We compared the effect of AMI-1 on lung adenocarcinoma (A549 cell line) suppression with the standard chemotherapeutic agent, cisplatin, by measuring cell viability using MTT assay, PMRT5/β-catenin expression via Western Blotting, the extent of cell migration through wound healing assay, and survival of cancer cells by performing cell cycle progression and Annexin-V staining assays.

Results and discussions Treating the cells with a combination of 10 μM AMI-1 and IC50 of Cisplatin (23.4 μM) significantly decreased cell viability at 24 and 48 hours. Moreover, treatment with both drugs at 48 hours led to a reduction in cell migration measured by the migration rate. AMI-1 induced G2/M arrest in A549 cells at 24 hours. This effect was enhanced in the combined treatment. Furthermore, A549 cells were unable to recycle again as they arrested at G1 after 48 hours of combination treatment. There was a minor cell death induction after 48 hours of treatment with both drugs. Neither PRMT5 nor β-catenin protein levels were affected due to the treatment. However, 48 hours treatment with AMI-1 alone or in combination with Cisplatin reduced the methylation of PRMT5- downstream target, Histone 4.

Conclusion Inhibition of the intracellular enzyme protein arginine methyltransferase 5 by AMI-1 potentiates the anti-cancer effect to cisplatin in the lung adenocarcinoma, with a promising potential role as an adjuvant therapy in lung cancer. The effect is likely mediated by methylation reduction of histone-4.

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PO-016 INHIBITION OF CELL PROLIFERATION BY ANTI-EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) APTAMER CONJUGATED CHITOSAN/SiRNA NANOPARTICLES

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Abstracts
gene therapy involved aptamer-EGFR and siRNA-RANKL is a promising therapy strategy. The support ing grant was from MESI-Québec (PSR-SIIRI, 2017–2020).

**PO-017** ANDROGEN DEPRIVATION AND OXIDATIVE PHOSPHORYLATION INHIBITION POSE SYNERGISTIC ANTITUMOR EFFECTS IN SUBSETS OF PROSTATE TUMOURS IN VITRO

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**Introduction** Cancer cells are able to survive oxidative phosphorylation (OXPHOS) inhibition by up-regulation of glycolysis. Androgens stimulate glycolysis in prostate cancer cells through activation of the androgen receptor (AR). Here we hypothesise that androgens might help subsets of prostate cancer cells to survive OXPHOS inhibition. In addition, the combined androgen signalling and OXPHOS inhibition might pose synergistic antitumour effects in vitro.

**Material and methods** The effects of suppressing OXPHOS with 100 ng/ml oligomycin in charcoal stripped serum media (CSS), before and after the addition of 40 ng/dl testosterone in VCAP, LNCaP, and LNCaP-C4-2B cells in vitro were evaluated. Tumour cell viability after 72 hours was estimated using MTT assay.

**Results and discussions** The addition of 100 ng/ml oligomycin to VCAP cells in a steroid-depleted environment (CSS) dramatically decreased cell viability compared to CSS alone (p<0.001). The addition of castrate testosterone levels (40 ng/dl) increased tumour cell viability both with and without the concurrent OXPHOS suppression (p<0.001 for both). VCAP cells are androgen-sensitive and harbour AR amplification. In LNCaP cells the addition of 100 ng/ml oligomycin in CSS resulted in a remarkable reduction in cell viability compared to CSS alone (p<0.001). Testosterone at 40 ng/ml increased cell viability compared to CSS alone, both with and without the concurrent OXPHOS inhibition (p<0.001 for both). The experiments were repeated using LNCaP-C4-2B cells. LNCaP-C4-2B cells are isogenic to LNCaP cells, but show persistent AR-mediated transcription even in androgen-deprived conditions. We found that the addition of 100 ng/ml oligomycin in CSS caused a smaller decrease in cell viability compared to LNCaP cells. Addition of 40 ng/dl testosterone significantly decreased the anti-tumour effects of OXPHOS inhibition (p<0.001). These in vitro results generate the hypothesis that active AR signalling might be involved in resistance towards the antitumor effects of OXPHOS inhibition.

**Conclusion** The combined androgen depletion and OXPHOS inhibition shows promising synergistic anti-tumour effects in vitro.

**PO-018** IMMUNOGENIC POTENTIAL OF COLD ATMOSPHERIC PLASMA FOR THE TREATMENT OF PANCREATIC CANCER

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**Introduction** Pancreatic ductal adenocarcinoma (PDAC) is a tumour with a fibroblastic stroma compartment that consists of pancreatic stellate cells (PSC) which play a complex role in supporting carcinogenesis, immunosuppression and therapy resistance. Therefore, the 5 year survival rate for PDAC patients remains below a disappointing 8%, stressing the need for new and more effective treatments. Recently, cold atmospheric plasma (CAP) has emerged as a potent treatment option for cancer. Although, CAP is being investigated for several years, the involvement of the immune system after CAP treatment remains poorly understood. The immunogenic cell death (ICD) concept describes that the killing of cancer cells leads to direct activation of the immune system through release of so-called ‘danger-associated molecular patterns’. ICD can be elicited by several physical means such as irradiation and photodynamic therapy, providing a rationale for the induction of ICD after CAP treatment. The aim of this study is to investigate the induction of a specific antitumour immune response after CAP treatment in PDAC, in vitro.

**Material and methods** Phosphate-buffered saline (PBS) was treated with CAP, generated by the kINPenIND, and subsequently added to monocultures of both pancreatic cancer cell (PCC) lines and PSC lines. To evaluate the four most important hallmarks of ICD, being membrane exposure of calreticulin, secretion of ATP and release of HMGB1 and type I interferon, the treatment parameters were optimised (i.e. treatment time, gas flow and gap distance) to obtain 50% cell death. The cellular difference in sensitivity for CAP treatment was assessed through cytotoxic analysis. After attaining the optimal treatment parameters, we investigated the translocation of calreticulin onto the cell surface with flow cytometry. ATP secretion was investigated with a bioluminescence assay, while ELISA was used to monitor the release of HMGB1 and interferon type I in the supernatants.

**Results and discussions** Our data report a cytotoxic effect of CAP treatment in vitro on both PCC and PSC. In both PCC and PSC our results show a significant expression of calreticulin after CAP treatment, together with a significant release of ATP in PCC, but not in PSC. The evaluation of other ICD hallmarks after CAP treatment is currently ongoing.

**Conclusion** We strongly believe that CAP therapy can be a good alternative for the treatment of PDAC. However, the results warrant further in vivo validation to refine the involvement of the immune system after CAP treatment.