Table 1 – Characteristics of the trials analyzed and data on survival according to prior treatment

Trial	Drug	Overall survival	
		Patients (*n*)	Median (mo)
Sunitinib			
CheckMate 025	Nivolumab vs everolimus	257 vs 261	23.6 vs 19.8
METEOR	Cabozantinib vs everolimus	135 vs 132	Not reported
Pazopanib			
CheckMate 025	Nivolumab vs everolimus	126 vs 136	Not reached vs 17.6
METEOR	Cabozantinib vs everolimus	88 vs 83	Not reported

nivolumab seem to reduce the risk of death in patients treated with prior pazopanib compared with sunitinib. These data will require further evaluation in prospective randomized clinical trials.

Conflicts of interest: The authors have nothing to disclose.

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Hyperpolarized 1-[^{13}C]-Pyruvate Magnetic Resonance Imaging Detects an Early Metabolic Response to Androgen Ablation Therapy in Prostate Cancer

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Hyperpolarized (HP) ^{13}C magnetic resonance spectroscopic imaging (MRSI) is a novel imaging technique that allows rapid and noninvasive monitoring of dynamic pathway-specific metabolic and physiologic processes [1] with unprecedented gain in sensitivity (10 000–200 000 fold increase) for imaging of ^{13}C-labeled biomolecules that are endogenous, nontoxic, and nonradioactive [2,3]. We previously reported the first-in-human phase 1 clinical study of HP [^{13}C]-pyruvate MRSI in patients with prostate cancer on active surveillance, and confirmed the feasibility of capturing regions of accelerated HP pyruvate-to-lactate flux in high-grade versus low-grade cancer versus benign tissue [4].

Here we describe the first results demonstrating the metabolic response to androgen deprivation therapy (ADT) using HP [^{13}C]-pyruvate MRSI. The patient presented with serum prostate-specific antigen (PSA) of 25.2 ng/ml and Gleason 4 + 5 prostate adenocarcinoma on biopsy. Cross-sectional imaging demonstrated metastases within the pelvic nodes and osseous structures. Baseline multiparametric (mp) ^{1}H MRI of the prostate (anatomic imaging, diffusion-weighted imaging [DWI], dynamic contrast-enhanced [DCE] imaging, and 3D ^{1}H MRSI) with HP [^{13}C]-pyruvate revealed a bulky tumor involving the left apex, mid gland, and base peripheral and transition zones, and right apex, mid gland, and base peripheral zone, measuring 4.5 × 1.5 × 5.1 cm^3. T2-weighted MRI showed a well-defined focus of low signal intensity (T2 score 5/5; Fig. 1A). The lesion also had marked restricted diffusion (DWI score 5/5; apparent diffusion coefficient [ADC] 930)

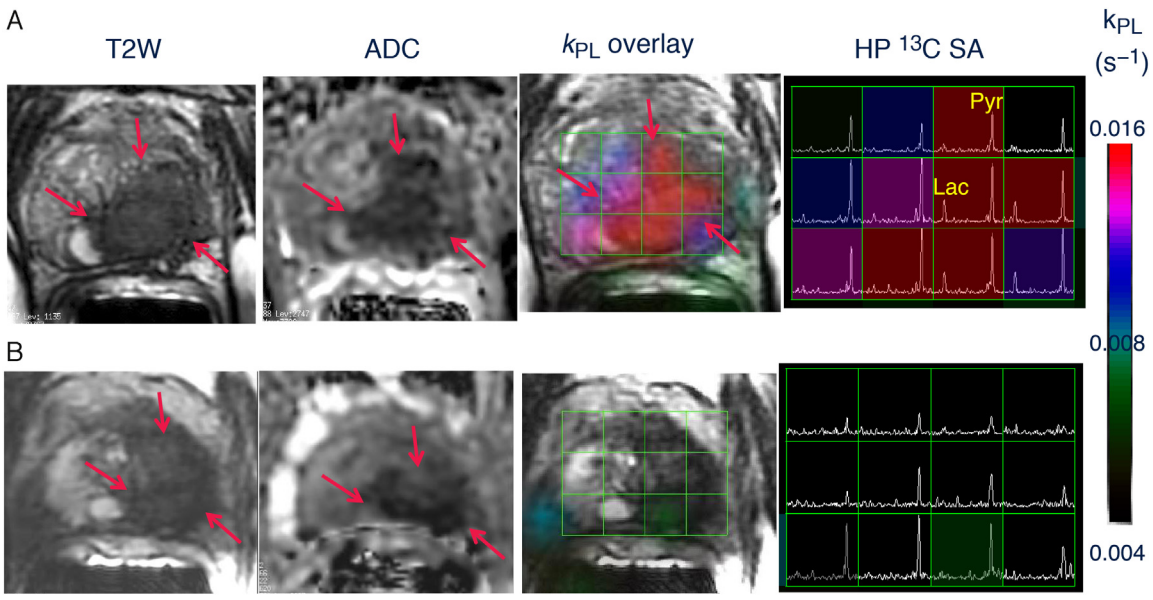

Fig. 1 – Representative axial T2-weighted (T2W) anatomic image and corresponding water apparent diffusion coefficient (ADC) image and T2W image with an overlaid pyruvate-to-lactate metabolic flux (k_{PL}) image and corresponding hyperpolarized (HP) ^{13}C spectral array (SA) for a 52-yr-old prostate cancer patient with extensive high-grade prostate cancer (A) before therapy and (B) 6 wk after initiation of androgen ablation and chemotherapy. Before treatment, the region of prostate cancer can be clearly seen (red arrows) as a reduction in signal on the T2W and ADC images, and increased HP lactate and associated k_{PL} flux on HP ^{13}C MRI. After initiation of androgen deprivation therapy there was a significant reduction in reduction in HP lactate and k_{PL} to normal levels, with only a modest treatment effect on prostate volume and ADC.

and was DCE-positive, with increased uptake and washout of contrast agent, and MRSI-positive, with elevated choline and reduced citrate on ^{1}H MRSI. The overall Prostate Imaging-Reporting and Data System v.2 score was 5.

Figure 1A shows the HP ^{13}C spectral array for the baseline scan, with markedly elevated lactate peaks within tumor-containing voxels. A color scale map of dynamic pyruvate-to-lactate metabolic flux (k_{PL}) values likewise shows markedly elevated flux levels in the tumor compared to adjacent normal tissue in the baseline HP [^{13}C]-pyruvate MRI.

At 6 wk after initiation of ADT, repeat imaging demonstrated nearly complete abrogation of elevated HP lactate peaks on HP ^{13}C MRI (Fig. 1B) and associated near complete diminution of intratumoral k_{PL} values on dynamic imaging (k_{PL} max 0.025 s^{-1} at baseline and 0.007 s^{-1} on follow-up). Notably, there was negligible change in size of tumor on T2-weighted MRI and only a modest change on ADC imaging, supporting the ability of HP ^{13}C MRI to detect early metabolic responses before such a response can be ascertained using standard radiographic criteria. Concordant with these findings, the patient subsequently achieved a marked clinical response, with an undetectable serum PSA nadir at 6 mo after ADT initiation.

This first patient example illustrates the potential of HP [^{13}C]-pyruvate imaging as a metabolic biomarker of response. Further clinical studies investigating the association between metabolic changes on HP ^{13}C MRI and response and resistance to treatment are ongoing.

Conflicts of interest: The authors have nothing to disclose.

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