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# Automated Body Composition Analyses Reveal Significant Associations with Mortality in Myeloma Patients Following Immunotherapy with Bispecific Antibodies

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**Background:** Body composition (BC) refers to the relative proportions of muscle, bone, subcutaneous and visceral adipose tissue for an individual. The association between obesity and a range of health conditions including cancer is well recognised but the Body Mass Index (BMI) commonly used in clinical assessments does not take into consideration the relative composition of skeletal muscle and adipose tissue and could be misleading in individuals with a high muscle mass. Furthermore, despite recognition of the significance of loss of skeletal muscle mass (sarcopenia) on outcomes in patients receiving chemotherapy, no standardised automated method currently exists to assess BC. Techniques used in estimating BC include body

impedance analysis, dual X-ray absorptiometry, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)-based methods. CT-based BC analysis done manually is often time-consuming hence the need for automated analyses based on deep learning algorithms. In this study, we compared BC data between relapsed/refractory myeloma (RRMM) patients receiving bispecific antibodies and controls, including correlation of BC in RRMM patients with outcomes such as cytokine release syndrome (CRS) and mortality. The primary aims were to investigate correlations of BC with risk of CRS, sarcopenia and survival of patients treated with bispecific antibodies.

**Methods:** Unselected patients with RRMM treated with bispecific antibodies and sex-matched controls comprising patients with smouldering myeloma (SMM) and Monoclonal Gammopathy of Undetermined Significance (MGUS) that had routine PET-CT scans were compared. Retrospective BC analyses were performed on whole-body CT components using Data Analysis Facility Suite (DAFS), a validated commercial software produced by Voronoi Health Analytics Inc. Each scan was manually checked by a clinician. This was part of the AUTOPILOT study, a collaboration between UCLH and the BiCyCLE team of St Mark's Academic Institute and The National Bowel Hospital, London, United Kingdom. Comparison of characteristics was performed including between subgroups based on outcomes such as CRS and mortality. Kaplan Meier analysis was performed to determine progression-free survival by bispecific antibody type.

**Results:** 43 RRMM patients that had a median of 5 (1-12) prior lines of therapy and received GPRC5D/CD3 bispecific antibodies (25, 58%) or BCMA/CD3 bispecifics (18, 42%) were assessed with 43 controls (32 male (74%),11 female (26%)). The control population was slightly older [RRMM median age (range); 60 (49 - 73) years, controls 66 (31 - 83) years]. BC analyses demonstrated no significant difference in Body Mass Index (BMI), total skeletal muscle, lung volumes as well as visceral and subcutaneous adipose tissue volumes between RRMM and controls. However, RRMM patients had significantly higher total cortical (p= 0.009) and trabecular bone volumes (p=0.02).

CRS occurred in 30 patients (70%) and was Grade 2 or less. There was no statistically significant difference between risk of CRS and total subcutaneous or visceral adipose tissue or total lung volumes. However, the patients that died during follow-up had significantly smaller total lung (p=0.04) and skeletal muscle volumes (p=0.01). These differences were also observed when stratified by patient's sex.

For both RRMM patients and controls, correlation analyses between BMI versus total subcutaneous and visceral adipose tissue revealed a stronger positive correlation with total subcutaneous tissue than visceral adipose tissue (Subcutaneous adipose tissue R squared=0.7294, Visceral adipose tissue R squared=0.2371). The observed median progression free survival

durations were 9 months and 7.5 months for recipients of GPRC5D/CD3 and BCMA/CD3 bispecific antibodies respectively.

**Conclusions:** In a relatively young, non-frail cohort of patients with RRMM treated with bispecific antibodies, low total skeletal muscle and lung volumes as measured by automated BC analysis were negative predictors of survival. Further evaluation of sarcopenia in MM is required as this may represent a potentially modifiable prognostic factor with prehabilitative/rehabilitative exercise and dietary interventions. BC analysis is therefore a useful tool to identify patients who may be at risk of mortality.

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