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Novel therapeutic drug combinations with CDK4/6 inhibitors, beyond ER+ve breast cancer

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The CDK4/6 – RB1 axis controls transition through the restriction point in the G1 phase of the cell cycle, and cancers frequently subvert the regulation of this axis to promote proliferation. CDK4/6 inhibition is a proven therapeutic strategy for estrogen receptor positive (ER+ve) breast cancers, with selective CDK4/6 inhibitors (palbociclib and ribociclib) demonstrating substantial improvements in progression free survival in phase two and three clinical trials (PALOMA1, PALOMA2, PALOMA3 and MONALEESA-2). There is considerable interest in exploring the role CDK4/6 inhibitors in drug combinations for patients with HER2 amplified breast groups and the TNBC subtypes. Triple negative breast cancer (TNBC) is an aggressive subtype of breast cancer associated with poor prognosis. Although TNBC may be sensitive to chemotherapy there is a substantial need to identify novel targeted therapeutic strategies. TNBC are a heterogeneous group of tumours with gene expression profiling identifying distinct subgroups, including luminal androgen receptor (LAR), mesenchymal stem like (MSL), mesenchymal (MES), and basal-like. *In vitro* data and *in vivo* data have shown that the LAR subtypes of breast cancer are highly sensitive to CDK4/6 inhibition and this is currently being tested in clinical trials. There is now growing amount of data suggesting that CDK4/6 inhibitor drug combinations, may have a role in breast cancer subtypes, beyond ER receptor positivity.

Speaker Biography

Uzma Saddia Asghar was awarded her MBBS (2004) and intercalated BSc in Neurosciences (2001) from University College London (UCL). She was awarded her MRCP in 2008 (London) and did her PhD at Breast Cancer now, Institute of Cancer, London as an Avon Clinical Research Fellow (2017). Her interests includes novel targeted therapeutic agents for breast cancer, inhibitors of cell cycle and PI3 kinase signaling pathway, immunotherapy and drug development and currently setting up these breast translational clinical trials at UCL.

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