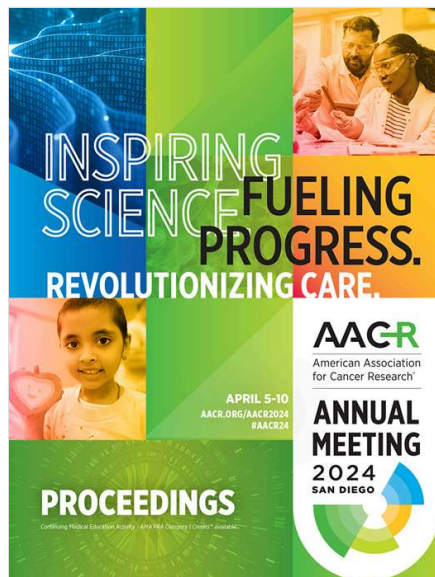




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POSTER PRESENTATIONS - PROFFERED ABSTRACTS | APRIL 05 2024

Abstract CT202: CSFctDNA as a surrogate for tumor tissue DNA in BC pts with CNS metastases: First results from the Brainstorm program (Oncodistinct 006) **FREE**

Nuria Kotecki; Diogo Martins-Branco; Guilherme Nader-Marta; Andrea Gombos; Philippe Barthelemy; Anthony Gonçalves; Edith Borcoman; Florian Clatot; Stéphane Holbrechts; Eleonora Stephane de Maio D'Esposito; Claire Cheymol; Vincent Vanhaudenarde; François Duhoux; Caroline Duhem; Paul Clement; Lore Decoster; Hannelore Denys; Florence Lefranc; Jean-Luc Canon; Joseph Gligorov; Luca Arecco; Nadège Kindt; Ahmad Awada



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Abstract

Background: Central nervous system (CNS) metastases display molecular alterations that differ from primary tumors and metastatic sites, which might confer special CNS sensitivity for targeted treatments. Brain biopsies are an invasive approach and liquid biopsies (LB) are therefore being investigated as a potential tool for detecting these molecular alterations in cerebrospinal fluid (CSF) ctDNA.

Methods: The BrainStorm program (NCT04109131) is an international, prospective, interventional study aiming to build a large clinico-pathological database to investigate the development of CNS metastases: (A) before the diagnosis; (B) at diagnosis; and (C) after the diagnosis of CNS metastases. Molecular landscape of CSFctDNA was analyzed and explored as a surrogate for CNS tumor tissue DNA using large next-generation sequencing panels in tumor tissue and tumor-informed targeted gene panels in LB (*OncoDEEP®/OncoFOLLOW®*) for patients (pts) included in Part (B).

Results: As of October 2023, CSF was available for 30 out of 67 pts included in Part (B) of the study and analyses were performed for 12 matched extra-CNS tumor, plasma and CSF samples. The 12 cases were derived from pts with breast cancer (BC) (luminal n=6; triple negative (TN) n=2; HER2-positive n=4) and among them 4 pts were diagnosed with leptomeningeal metastases (LM). CSFctDNA was detectable in 7 out of the 12 CSF samples (58%) and in 3 out of 4 pts with LM (75%). In pts with detectable CSFctDNA, detection rate for known pathogenic molecular alterations was 80% (**Table 1**). No safety concerns from lumbar puncture were identified.

Conclusion: The use of CSFctDNA as a surrogate for tumor tissue DNA in CNS metastases appears to be a feasible and safe approach. Clinically actionable alterations have been identified in CSFctDNA of pts with BC. Further results will be presented at a later stage.

TABLE 1: NAND Table 1: Pathogenic molecular alterations in matched tumor, plasma and CSF from pts with detectable CSFctDNA

Tumor type	Extra-CNS tumor tissue	Plasma	CSF
TNBC	PIK3Ca pH1047R	PIK3Ca pH1047R	PIK3Ca pH1047R
Luminal BC	PIK3Ca Q546R	PIK3Ca Q546R	PIK3Ca Q546R
Luminal (LM)	None	KRAS pG13D	None
Luminal BC	BRCA2 p.Y1655, PIK3CA pE545K	BRCA2 pY1655, PIK3CA pE545K	BRCA2 pY1655, PIK3CA pE545K
TNBC (LM)	None	None	None
Luminal (LM)	ESR1 D538G, PIK3CA H1047R	ESR1 D538G, PIK3CA H1047R	ESR1 D538G, PIK3CA H1047R
HER2-positive BC	ErbB2 amplification	None	None

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