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OBJECTIVE

To investigate the mutational profiling associated with Brazilian mucinous adenocarcinoma of ovary.

METHODS

We included 47 patients from Barretos Cancer Hospital, from 2009 and 2015. HER2 amplification was evaluated by immunohistochemistry (IHC) and/or in situ hybridization (FISH). In addition, the hotspots regions of the KRAS (codons 12 and 13) were screened by PCR followed by direct Sanger sequencing. Finally, to provide a comprehensive assessment of 15 genes that are commonly mutated in solid tumors we performed the NGS-based mutation analysis using the Illumina TruSight Tumor 15 panel on MiSeq instrument (Illumina, USA).

RESULTS

HER2 IHC was performed in 28 samples and the negative staining was found in 26 (92.8%). In 2 samples (7.7%), because the IHC was inconclusive (moderate expression), we performed hybridization in situ (FISH) and found HER2 amplification in both. Clinically, both cases had pseudomixoma peritonei and 1 had disease recurrence. To KRAS Sanger sequencing, due to DNA quality issues, conclusive results were obtained in 26 cases. Interestingly, KRAS mutations were found in 11 samples (42.3%), all in codon 12, and were associated with no recurrence (p=0.036). By Illumina TruSight Tumor 15 panel we evaluated 16 samples. All samples showed at least one mutation in one gene and the most mutated genes were: TP53 and KRAS (10 mutations in each), BRAF (4) and HER2 and PIK3CA (1).

Table 1: Summary of results to HER2 IHC, KRAS Sanger sequencing and Illumina NGS TruSight Tumor 15.

ID	HER2 IHC	KRAS Sanger Sequencing	Illumina NGS
45	neg (0)	G12V	Not avaiable
16	neg (0)	G12A	Not avaiable
8	neg (1)	WT	Not avaiable
25	neg (0)	Failed	Not avaiable
19	neg (0)	WT	KRAS - c.183A>C and TP53 - c.524G>A
20	neg (0)	WT	Not avaiable
12	neg (0)	WT	PIK3CA - c.1634A>G
40	neg (0)	Failed	Not avaiable
37	neg (0)	WT	TP53 - c.665C>T
5	No core	Failed	Not avaiable
7	neg (0)	G12A	KRAS - c.35G>A and TP53 - c.559+1G>A
46	neg (0)	WT	Not avaiable
10	neg (0)	G12A	KRAS - c.35G>T and TP53 - c.374C>A
38	neg (0)	G12A	KRAS -c.35G>T and TP53 - c.892G>T
24	neg (0)	G12A	KRAS - c.35G>T and TP53 - c.469G>T
15	doubt (2+)	WT	TP53 - c.709_711delATG
43	neg (0)	G12A	KRAS- c.34G>C
27	neg (1)	WT	BRAF - c.1799T>A and ERBB2 - c.2039C>T
29	neg (0)	G12A	KRAS - c.35G>T
31	neg (0)	WT	BRAF - c.1801A>G
30	No tumor	G12A	Not avaiable
34	No tumor	WT	Not avaiable
35	neg (1)	G12C	Not avaiable
17	neg (0)	G12C	KRAS- c.34G>T and TP53 - c.817C>T
6	neg (0)	Failed	Not avaiable
26	neg (0)	WT	BRAF - c.1799T>A
41	neg (0)	Failed	Not avaiable
32	doubt (2+)	WT	BRAF - c.1808G>A , KRAS - c.35G>T , KRAS - c.448C>T and TP53 - c.796G>A
23	No tumor	WT	TP53 - c.524G>A
2	neg (0)	Failed	Not avaiable
13	neg (0)	WT	Not avaiable
18	neg (0)	WT	Not avaiable

CONCLUSIONS

We identified the mutational profiling associated with Brazilian mucinous adenocarcinoma of ovary highlighting its genomic heterogeneity and potential therapeutic targets that could be investigated in future new clinical trials.