

72-YEAR-OLD FEMALE PATIENT

TRANSVERSE COLON PRIMARY AND SOLITARY LIVER AND LUNG METASTASIS

PIK3CA mutations may not yet be directly targetable in colon cancer; however, these mutations still carry impactful actionable therapeutic decisions.

PIK3CA mutations play a role in guiding individual decisions regarding the effectiveness of anti-EGFR monoclonal antibodies. With the availability of broad next-generation sequencing (NGS) testing, PIK3CA mutations are now identified as one of several pathways beyond the basic RAS/RAF resistance pathways that predicts cetuximab or panitumumab resistance.

PIK3CA mutations also have a predictive impact of a liver radioembolization benefit in treating colorectal liver metastasis. Patients with chemotherapy refractory colon liver metastases with PIK3CA mutations achieved a much higher response rate and markedly longer local control than colon cancers without PIK3CA mutations.

The most dramatic survival benefit of PIK3CA mutations is with simple aspirin use. Published back in 2012, the regular use of aspirin after definitive cancer treatment for PIK3CA mutated colon cancers had a dramatic reduction in cancer-specific and overall mortality, whereas the use of aspirin had no impact in the PIK3CA wild type cancers. So simple but so impactful!

The evolution of liquid biopsy NGS technology is now readily available and can easily overcome the tissue heterogeneity limitations and tissue acquisition barriers to accurately identify the tumor biology that can then guide a more precise and better treatment for patients.

SUMMARY OF RESULTS

Gene(s) Tested:	50
Alteration(s) Detected:	3
FDA-Approved Targeted Therapies:	2
Additional Therapies:	0
Open Clinical Trials: see pg 6	48

The following 50 genes were tested: ABL1, AKT1, ALK, APC, ATM, BRAF, CDH1, CDKN2A, CSF1R, CTNNB1, EGFR, ERBB2, ERBB4, EZR, FGF3, FGF4, FGF19, FGF20, FGF21, FGF22, FGF23, FGF30, FGF31, FGF32, FGF33, FGF34, FGF35, FGF36, FGF37, FGF38, FGF39, FGF40, FGF41, FGF42, FGF43, FGF44, FGF45, FGF46, FGF47, FGF48, FGF49, FGF50, FGF51, FGF52, FGF53, FGF54, FGF55, FGF56, FGF57, FGF58, FGF59, FGF60, FGF61, FGF62, FGF63, FGF64, FGF65, FGF66, FGF67, FGF68, FGF69, FGF70, FGF71, FGF72, FGF73, FGF74, FGF75, FGF76, FGF77, FGF78, FGF79, FGF80, FGF81, FGF82, FGF83, FGF84, FGF85, FGF86, FGF87, FGF88, FGF89, FGF90, FGF91, FGF92, FGF93, FGF94, FGF95, FGF96, FGF97, FGF98, FGF99, FGF100, FGF101, FGF102, FGF103, FGF104, FGF105, FGF106, FGF107, FGF108, FGF109, FGF110, FGF111, FGF112, FGF113, FGF114, FGF115, FGF116, FGF117, FGF118, FGF119, FGF120, FGF121, FGF122, FGF123, FGF124, FGF125, FGF126, FGF127, FGF128, FGF129, FGF130, FGF131, FGF132, FGF133, FGF134, FGF135, FGF136, FGF137, FGF138, FGF139, FGF140, FGF141, FGF142, FGF143, FGF144, FGF145, FGF146, FGF147, FGF148, FGF149, FGF150, FGF151, FGF152, FGF153, FGF154, FGF155, FGF156, FGF157, FGF158, FGF159, FGF160, FGF161, FGF162, FGF163, FGF164, FGF165, FGF166, FGF167, FGF168, FGF169, FGF170, FGF171, FGF172, FGF173, FGF174, FGF175, FGF176, FGF177, FGF178, FGF179, FGF180, FGF181, FGF182, FGF183, FGF184, FGF185, FGF186, FGF187, FGF188, FGF189, FGF190, FGF191, FGF192, FGF193, FGF194, FGF195, FGF196, FGF197, FGF198, FGF199, FGF200, FGF201, FGF202, FGF203, FGF204, FGF205, FGF206, FGF207, FGF208, FGF209, FGF210, FGF211, FGF212, FGF213, FGF214, FGF215, FGF216, FGF217, FGF218, FGF219, FGF220, FGF221, FGF222, FGF223, FGF224, FGF225, FGF226, FGF227, FGF228, FGF229, FGF230, FGF231, FGF232, FGF233, FGF234, FGF235, FGF236, FGF237, FGF238, FGF239, FGF240, FGF241, FGF242, FGF243, FGF244, FGF245, FGF246, FGF247, FGF248, FGF249, FGF250, FGF251, FGF252, FGF253, FGF254, FGF255, FGF256, FGF257, FGF258, FGF259, FGF260, FGF261, FGF262, FGF263, FGF264, FGF265, FGF266, FGF267, FGF268, FGF269, FGF270, FGF271, FGF272, FGF273, FGF274, FGF275, FGF276, FGF277, FGF278, FGF279, FGF280, FGF281, FGF282, FGF283, FGF284, FGF285, FGF286, FGF287, FGF288, FGF289, FGF290, FGF291, FGF292, FGF293, FGF294, FGF295, FGF296, FGF297, FGF298, FGF299, FGF300, FGF301, FGF302, FGF303, FGF304, FGF305, FGF306, FGF307, FGF308, FGF309, FGF310, FGF311, FGF312, FGF313, FGF314, FGF315, FGF316, FGF317, FGF318, FGF319, FGF320, FGF321, FGF322, FGF323, FGF324, FGF325, FGF326, FGF327, FGF328, FGF329, FGF330, FGF331, FGF332, FGF333, FGF334, FGF335, FGF336, FGF337, FGF338, FGF339, FGF340, FGF341, FGF342, FGF343, FGF344, FGF345, FGF346, FGF347, FGF348, FGF349, FGF350, FGF351, FGF352, FGF353, FGF354, FGF355, FGF356, FGF357, FGF358, FGF359, FGF360, FGF361, FGF362, FGF363, FGF364, FGF365, FGF366, FGF367, FGF368, FGF369, FGF370, FGF371, FGF372, FGF373, FGF374, FGF375, FGF376, FGF377, FGF378, FGF379, FGF380, FGF381, FGF382, FGF383, FGF384, FGF385, FGF386, FGF387, FGF388, FGF389, FGF390, FGF391, FGF392, FGF393, FGF394, FGF395, FGF396, FGF397, FGF398, FGF399, FGF400, FGF401, FGF402, FGF403, FGF404, FGF405, FGF406, FGF407, FGF408, FGF409, FGF410, FGF411, FGF412, FGF413, FGF414, FGF415, FGF416, FGF417, FGF418, FGF419, FGF420, FGF421, FGF422, FGF423, FGF424, FGF425, FGF426, FGF427, FGF428, FGF429, FGF430, FGF431, FGF432, FGF433, FGF434, FGF435, FGF436, FGF437, FGF438, FGF439, FGF440, FGF441, FGF442, FGF443, FGF444, FGF445, FGF446, FGF447, FGF448, FGF449, FGF450, FGF451, FGF452, FGF453, FGF454, FGF455, FGF456, FGF457, FGF458, FGF459, FGF460, FGF461, FGF462, FGF463, FGF464, FGF465, FGF466, FGF467, FGF468, FGF469, FGF470, FGF471, FGF472, FGF473, FGF474, FGF475, FGF476, FGF477, FGF478, FGF479, FGF480, FGF481, FGF482, FGF483, FGF484, FGF485, FGF486, FGF487, FGF488, FGF489, FGF490, FGF491, FGF492, FGF493, FGF494, FGF495, FGF496, FGF497, FGF498, FGF499, FGF500, FGF501, FGF502, FGF503, FGF504, FGF505, FGF506, FGF507, FGF508, FGF509, FGF510, FGF511, FGF512, FGF513, FGF514, FGF515, FGF516, FGF517, FGF518, FGF519, FGF520, FGF521, FGF522, FGF523, FGF524, FGF525, FGF526, FGF527, FGF528, FGF529, FGF530, FGF531, FGF532, FGF533, FGF534, FGF535, FGF536, FGF537, FGF538, FGF539, FGF540, FGF541, FGF542, FGF543, FGF544, FGF545, FGF546, FGF547, FGF548, FGF549, FGF550, FGF551, FGF552, FGF553, FGF554, FGF555, FGF556, FGF557, FGF558, FGF559, FGF560, FGF561, FGF562, FGF563, FGF564, FGF565, FGF566, FGF567, FGF568, FGF569, FGF570, FGF571, FGF572, FGF573, FGF574, FGF575, FGF576, FGF577, FGF578, FGF579, FGF580, FGF581, FGF582, FGF583, FGF584, FGF585, FGF586, FGF587, FGF588, FGF589, FGF590, FGF591, FGF592, FGF593, FGF594, FGF595, FGF596, FGF597, FGF598, FGF599, FGF600, FGF601, FGF602, FGF603, FGF604, FGF605, FGF606, FGF607, FGF608, FGF609, FGF610, FGF611, FGF612, FGF613, FGF614, FGF615, FGF616, FGF617, FGF618, FGF619, FGF620, FGF621, FGF622, FGF623, FGF624, FGF625, FGF626, FGF627, FGF628, FGF629, FGF630, FGF631, FGF632, FGF633, FGF634, FGF635, FGF636, FGF637, FGF638, FGF639, FGF640, FGF641, FGF642, FGF643, FGF644, FGF645, FGF646, FGF647, FGF648, FGF649, FGF650, FGF651, FGF652, FGF653, FGF654, FGF655, FGF656, FGF657, FGF658, FGF659, FGF660, FGF661, FGF662, FGF663, FGF664, FGF665, FGF666, FGF667, FGF668, FGF669, FGF670, FGF671, FGF672, FGF673, FGF674, FGF675, FGF676, FGF677, FGF678, FGF679, FGF680, FGF681, FGF682, FGF683, FGF684, FGF685, FGF686, FGF687, FGF688, FGF689, FGF690, FGF691, FGF692, FGF693, FGF694, FGF695, FGF696, FGF697, FGF698, FGF699, FGF700, FGF701, FGF702, FGF703, FGF704, FGF705, FGF706, FGF707, FGF708, FGF709, FGF710, FGF711, FGF712, FGF713, FGF714, FGF715, FGF716, FGF717, FGF718, FGF719, FGF720, FGF721, FGF722, FGF723, FGF724, FGF725, FGF726, FGF727, FGF728, FGF729, FGF730, FGF731, FGF732, FGF733, FGF734, FGF735, FGF736, FGF737, FGF738, FGF739, FGF740, FGF741, FGF742, FGF743, FGF744, FGF745, FGF746, FGF747, FGF748, FGF749, FGF750, FGF751, FGF752, FGF753, FGF754, FGF755, FGF756, FGF757, FGF758, FGF759, FGF760, FGF761, FGF762, FGF763, FGF764, FGF765, FGF766, FGF767, FGF768, FGF769, FGF770, FGF771, FGF772, FGF773, FGF774, FGF775, FGF776, FGF777, FGF778, FGF779, FGF780, FGF781, FGF782, FGF783, FGF784, FGF785, FGF786, FGF787, FGF788, FGF789, FGF790, FGF791, FGF792, FGF793, FGF794, FGF795, FGF796, FGF797, FGF798, FGF799, FGF800, FGF801, FGF802, FGF803, FGF804, FGF805, FGF806, FGF807, FGF808, FGF809, FGF810, FGF811, FGF812, FGF813, FGF814, FGF815, FGF816, FGF817, FGF818, FGF819, FGF820, FGF821, FGF822, FGF823, FGF824, FGF825, FGF826, FGF827, FGF828, FGF829, FGF830, FGF831, FGF832, FGF833, FGF834, FGF835, FGF836, FGF837, FGF838, FGF839, FGF840, FGF841, FGF842, FGF843, FGF844, FGF845, FGF846, FGF847, FGF848, FGF849, FGF850, FGF851, FGF852, FGF853, FGF854, FGF855, FGF856, FGF857, FGF858, FGF859, FGF860, FGF861, FGF862, FGF863, FGF864, FGF865, FGF866, FGF867, FGF868, FGF869, FGF870, FGF871, FGF872, FGF873, FGF874, FGF875, FGF876, FGF877, FGF878, FGF879, FGF880, FGF881, FGF882, FGF883, FGF884, FGF885, FGF886, FGF887, FGF888, FGF889, FGF890, FGF891, FGF892, FGF893, FGF894, FGF895, FGF896, FGF897, FGF898, FGF899, FGF900, FGF901, FGF902, FGF903, FGF904, FGF905, FGF906, FGF907, FGF908, FGF909, FGF910, FGF911, FGF912, FGF913, FGF914, FGF915, FGF916, FGF917, FGF918, FGF919, FGF920, FGF921, FGF922, FGF923, FGF924, FGF925, FGF926, FGF927, FGF928, FGF929, FGF930, FGF931, FGF932, FGF933, FGF934, FGF935, FGF936, FGF937, FGF938, FGF939, FGF940, FGF941, FGF942, FGF943, FGF944, FGF945, FGF946, FGF947, FGF948, FGF949, FGF950, FGF951, FGF952, FGF953, FGF954, FGF955, FGF956, FGF957, FGF958, FGF959, FGF960, FGF961, FGF962, FGF963, FGF964, FGF965, FGF966, FGF967, FGF968, FGF969, FGF970, FGF971, FGF972, FGF973, FGF974, FGF975, FGF976, FGF977, FGF978, FGF979, FGF980, FGF981, FGF982, FGF983, FGF984, FGF985, FGF986, FGF987, FGF988, FGF989, FGF990, FGF991, FGF992, FGF993, FGF994, FGF995, FGF996, FGF997, FGF998, FGF999, FGF1000, FGF1001, FGF1002, FGF1003, FGF1004, FGF1005, FGF1006, FGF1007, FGF1008, FGF1009, FGF1010, FGF1011, FGF1012, FGF1013, FGF1014, FGF1015, FGF1016, FGF1017, FGF1018, FGF1019, FGF1020, FGF1021, FGF1022, FGF1023, FGF1024, FGF1025, FGF1026, FGF1027, FGF1028, FGF1029, FGF1030, FGF1031, FGF1032, FGF1033, FGF1034, FGF1035, FGF1036, FGF1037, FGF1038, FGF1039, FGF1040, FGF1041, FGF1042, FGF1043, FGF1044, FGF1045, FGF1046, FGF1047, FGF1048, FGF1049, FGF1050, FGF1051, FGF1052, FGF1053, FGF1054, FGF1055, FGF1056, FGF1057, FGF1058, FGF1059, FGF1060, FGF1061, FGF1062, FGF1063, FGF1064, FGF1065, FGF1066, FGF1067, FGF1068, FGF1069, FGF1070, FGF1071, FGF1072, FGF1073, FGF1074, FGF1075, FGF1076, FGF1077, FGF1078, FGF1079, FGF1080, FGF1081, FGF1082, FGF1083, FGF1084, FGF1085, FGF1086, FGF1087, FGF1088, FGF1089, FGF1090, FGF1091, FGF1092, FGF1093, FGF1094, FGF1095, FGF1096, FGF1097, FGF1098, FGF1099, FGF1100, FGF1101, FGF1102, FGF1103, FGF1104, FGF1105, FGF1106, FGF1107, FGF1108, FGF1109, FGF1110, FGF1111, FGF1112, FGF1113, FGF1114, FGF1115, FGF1116, FGF1117, FGF1118, FGF1119, FGF1120, FGF1121, FGF1122, FGF1123, FGF1124, FGF1125, FGF1126, FGF1127, FGF1128, FGF1129, FGF1130, FGF1131, FGF1132, FGF1133, FGF1134, FGF1135, FGF1136, FGF1137, FGF1138, FGF1139, FGF1140, FGF1141, FGF1142, FGF1143, FGF1144, FGF1145, FGF1146, FGF1147, FGF1148, FGF1149, FGF1150, FGF1151, FGF1152, FGF1153, FGF1154, FGF1155, FGF1156, FGF1157, FGF1158, FGF1159, FGF1160, FGF1161, FGF1162, FGF1163, FGF1164, FGF1165, FGF1166, FGF1167, FGF1168, FGF1169, FGF1170, FGF1171, FGF1172, FGF1173, FGF1174, FGF1175, FGF1176, FGF1177, FGF1178, FGF1179, FGF1180, FGF1181, FGF1182, FGF1183, FGF1184, FGF1185, FGF1186, FGF1187, FGF1188, FGF1189, FGF1190, FGF1191, FGF1192, FGF1193, FGF1194, FGF1195, FGF1196, FGF1197, FGF1198, FGF1199, FGF1200, FGF1201, FGF1202, FGF1203, FGF1204, FGF1205, FGF1206, FGF1207, FGF1208, FGF1209, FGF1210, FGF1211, FGF1212, FGF1213, FGF1214, FGF1215, FGF1216, FGF1217, FGF1218, FGF1219, FGF1220, FGF1221, FGF1222, FGF1223, FGF1224, FGF1225, FGF1226, FGF1227, FGF1228, FGF1229, FGF1230, FGF1231, FGF1232, FGF1233, FGF1234, FGF1235, FGF1236, FGF1237, FGF1238, FGF1239, FGF1240, FGF1241, FGF1242, FGF1243, FGF1244, FGF1245, FGF1246, FGF1247, FGF1248, FGF1249, FGF1250, FGF1251, FGF1252, FGF1253, FGF1254, FGF1255, FGF1256, FGF1257, FGF1258, FGF1259, FGF1260, FGF1261, FGF1262, FGF1263, FGF1264, FGF1265, FGF1266, FGF1267, FGF1268, FGF1269, FGF1270, FGF1271, FGF1272, FGF1273, FGF1274, FGF1275, FGF1276, FGF1277, FGF1278, FGF1279, FGF1280, FGF1281, FGF1282, FGF1283, FGF1284, FGF1285, FGF1286, FGF1287, FGF1288, FGF1289, FGF1290, FGF1291, FGF1292, FGF1293, FGF1294, FGF1295, FGF1296, FGF1297, FGF1298, FGF1299, FGF1300, FGF1301, FGF1302, FGF1303, FGF1304, FGF1305, FGF1306, FGF1307, FGF1308, FGF1309, FGF1310, FGF1311, FGF1312, FGF1313, FGF1314, FGF1315, FGF1316, FGF1317, FGF1318, FGF1319, FGF1320, FGF1321, FGF1322, FGF1323, FGF1324, FGF1325, FGF1326, FGF1327, FGF1328, FGF1329, FGF1330, FGF1331, FGF1332, FGF1333, FGF1334, FGF1335, FGF1336, FGF1337, FGF1338, FGF1339, FGF1340, FGF1341, FGF1342, FGF1343, FGF1344, FGF1345, FGF1346, FGF1347, FGF1348, FGF1349, FGF1350, FGF1351, FGF1352, FGF1353, FGF1354, FGF1355, FGF1356, FGF1357, FGF1358, FGF1359, FGF1360, FGF1361, FGF1362, FGF1363, FGF1364, FGF1365, FGF1366, FGF1367, FGF1368, FGF1369, FGF1370, FGF1371, FGF1372, FGF1373, FGF1374, FGF1375, FGF1376, FGF1377, FGF1378, FGF1379, FGF1380, FGF1381, FGF1382, FGF1383, FGF1384, FGF1385, FGF1386, FGF1387, FGF1388, FGF1389, FGF1390, FGF1391, FGF1392, FGF1393, FGF1394, FGF1395, FGF1396, FGF1397, FGF1398, FGF1399, FGF1400, FGF1401, FGF1402, FGF1403, FGF1404, FGF1405, FGF1406, FGF1407, FGF1408, FGF1409, FGF1410, FGF1411, FGF1412, FGF1413, FGF1414, FGF1415, FGF1416, FGF1417, FGF1418, FGF1419, FGF1420, FGF1421, FGF1422, FGF1423, FGF1424, FGF1425, FGF1426, FGF1427, FGF1428, FGF1429, FGF1430, FGF1431, FGF1432, FGF1433, FGF1434, FGF1435, FGF1436, FGF1437, FGF1438, FGF1439, FGF1440, FGF1441, FGF1442, FGF1443, FGF1444, FGF1445, FGF1446, FGF1447, FGF1448, FGF1449, FGF1450, FGF1451, FGF1452, FGF1453, FGF1454, FGF1455, FGF1456, FGF1457, FGF1458, FGF1459, FGF1460, FGF1461, FGF1462, FGF1463, FGF1464, FGF1465, FGF1466, FGF1467, FGF1468, FGF1469, FGF1470, FGF1471, FGF1472, FGF1473, FGF1474, FGF1475, FGF1476, FGF1477, FGF1478, FGF1479, FGF1480, FGF1481, FGF1482, FGF1483, FGF1484, FGF1485, FGF1486, FGF1487, FGF1488, FGF1489, FGF1490, FGF1491, FGF1492, FGF1493, FGF1494, FGF1495, FGF1496, FGF1497, FGF1498, FGF1499, FGF1500, FGF1501, FGF1502, FGF1503, FGF1504, FGF1505, FGF1506, FGF1507, FGF1508, FGF1509, FGF1510, FGF1511, FGF1512, FGF1513, FGF1514, FGF1515, FGF1516, FGF1517, FGF1518, FGF1519, FGF1520, FGF1521, FGF1522, FGF1523, FGF1524, FGF1525, FGF1526, FGF1527, FGF1528, FGF1529, FGF1530, FGF1531, FGF1532, FGF1533, FGF1534, FGF1535, FGF1536, FGF1537, FGF1538, FGF1539, FGF1540, FGF1541, FGF1542, FGF1543, FGF1544, FGF1545, FGF1546, FGF1547, FGF1548, FGF1549, FGF1550, FGF1551, FGF1552, FGF1553, FGF1554, FGF1555, FGF1556, FGF1557, FGF1558, FGF1559, FGF1560, FGF1561, FGF1562, FGF1563, FGF1564, FGF1565, FGF1566, FGF1567, FGF1568, FGF1569, FGF1570, FGF1571, FGF1572, FGF1573, FGF1574, FGF1575, FGF1576, FGF1577, FGF1578, FGF1579, FGF1580, FGF1581, FGF1582, FGF1583, FGF1584, FGF1585, FGF1586, FGF1587, FGF1588, FGF1589, FGF1590, FGF1591, FGF1592, FGF1593, FGF1594, FGF1595, FGF1596, FGF1597, FGF1598, FGF1599, FGF1600, FGF1601, FGF1602, FGF1603, FGF1604, FGF1605, FGF1606, FGF1607, FGF1608, FGF1609, FGF1610, FGF1611, FGF1612, FGF1613, FGF1614, FGF1615, FGF1616, FGF1617, FGF1618, FGF1619, FGF1620, FGF1621, FGF1622, FGF1623, FGF1624, FGF1625, FGF1626, FGF1627, FGF1628, FGF1629, FGF1630, FGF1631, FGF1632, FGF1633, FGF1634, FGF1635, FGF1636, FGF1637, FGF1638, FGF1639, FGF1640, FGF1641, FGF1642, FGF1643, FGF1644, FGF1645, FGF1646, FGF1647, FGF1648, FGF1649, FGF1650, FGF1651, FGF1652, FGF1653, FGF1654, FGF1655, FGF1656, FGF1657, FGF1658, FGF1659, FGF1660, FGF1661, FGF1662, FGF1663, FGF1664, FGF1665, FGF1666, FGF1667, FGF1668, FGF1669, FGF1670, FGF1671, FGF1672, FGF1673, FGF1674, FGF1675, FGF1676, FGF1677, FGF1678, FGF1679, FGF1680, FGF1681, FGF1682, FGF1683, FGF1684, FGF1685, FGF1686, FGF1687, FGF1688, FGF1689, FGF1690, FGF1691, FGF1692, FGF1693, FGF1694, FGF1695, FGF1696, FGF1697, FGF1698, FGF1699, FGF1700, FGF1701, FGF1702, FGF1703, FGF1704, FGF1705, FGF1706, FGF1707, FGF1708, FGF1709, FGF1710, FGF1711, FGF1712, FGF1713, FGF1714, FGF1715, FGF1716, FGF1717, FGF1718, FGF1719, FGF1720, FGF1721, FGF1722, FGF1723, FGF1724, FGF1725, FGF1726, FGF1727, FGF1728, FGF1729, FGF1730, FGF1731, FGF1732, FGF1733, FGF1734, FGF1735, FGF1736, FGF1737, FGF1738, FGF1739, FGF1740, FGF1741, FGF1742, FGF1743, FGF1744, FGF1745, FGF1746, FGF1747, FGF1748, FGF1749, FGF1750, FGF1751, FGF1752, FGF1753, FGF1754, FGF1755, FGF1756, FGF1757, FGF1758, FGF1759, FGF1760, FGF1761, FGF1762, FGF1763, FGF1764, FGF1765, FGF1766, FGF1767, FGF1768, FGF1769, FGF1770, FGF1771, FGF1772, FGF1773, FGF1774, FGF1775, FGF1776, FGF1777, FGF1778, FGF1779, FGF1780, FGF1781, FGF1782, FGF1783, FGF1784, FGF1785, FGF1786, FGF1787, FGF1788, FGF1789, FGF1790, FGF1791, FGF1792, FGF1793, FGF1794, FGF1795, FGF1796, FGF1797, FGF1798, FGF1799, FGF1800, FGF1801, FGF1802, FGF1803, FGF1804, FGF1805, FGF1806, FGF1807, FGF1808, FGF1809, FGF1810, FGF1811, FGF1812, FGF1813, FGF1814, FGF1815, FGF1816, FGF1817, FGF1818, FGF1819, FGF1820, FGF1821, FGF1822, FGF1823, FGF1824, FGF1825, FGF1826, FGF1827, FGF1828, FGF1829, FGF1830, FGF1831, FGF1832, FGF1833, FGF1834, FGF18

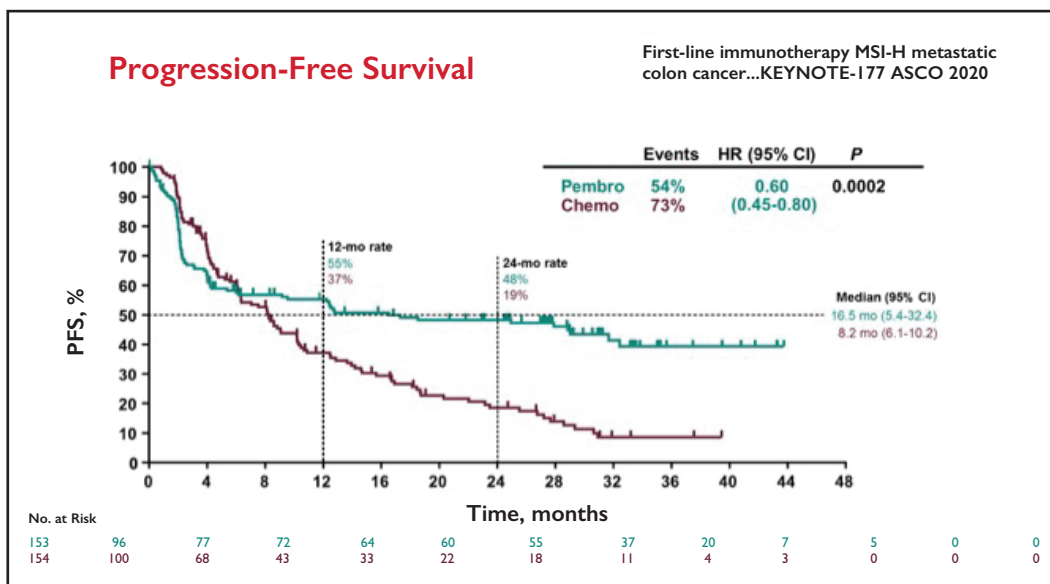
## 53-YEAR-OLD MALE PATIENT MSI-H METASTATIC COLON CANCER

Microsatellite instability high (MSI-H) cancers carry a unique tumor biology with chemotherapy resistance yet anti-angiogenesis and immune checkpoint inhibition (ICI) therapeutic sensitivity. MSI-H cancers clearly need to be treated differently.

Adjuvant 5-fluorouracil-based chemotherapy has long been known to be ineffective in patients with MSI-H colon cancers who would otherwise benefit from adjuvant chemotherapy. MSI-H colon cancers demonstrated a better benefit with the addition of anti-angiogenesis therapy with bevacizumab in both the metastatic treatment setting but also in the adjuvant setting. In the KRAS wild-type metastatic trial CALGB/SWOG 80405, the addition of bevacizumab to the mFOLFOX6 chemotherapy backbone more than doubled the median overall survival compared to cetuximab in MSI-H patients, with no biologic agent differential impact in the MSS patients. Likewise, in the adjuvant NSABP-08 trial, the addition of bevacizumab to adjuvant mFOLFOX6 was of no benefit in the overall group. However, in patients with mismatch repair deficiency colon cancers and the unique MSI tumor biology, there was significant survival benefit of adding bevacizumab to the adjuvant chemotherapy.

Most notable now is the sensitivity of MSI-H cancers to immune therapy with ICIs. The second-line FDA tissue-agnostic approval of anti-PD-1 therapy in 2017—solely based upon the MSI-H tumor biology irrespective of the anatomical tissue of origin—has now evolved into first-line FDA approval of immune therapy in metastatic MSI-H colon cancers in 2020. At ASCO 2020, single-agent pembrolizumab in MSI-H colorectal cancer achieved a much higher response rate and progression free survival with marked durability compared to standard chemotherapy. This same marked benefit of ICI in MSI-H colorectal cancer patients has now entered into earlier stage use, with one study achieving a 100% major pathologic response!

It is vitally important that MSI is assessed on all colorectal cancers. MSI-H is a tumor biology with dramatic benefit when treated with immune therapy. MSI status can now easily and quickly be assessed by a liquid biopsy. Clearance of the plasma MSI is also a dynamic marker to monitor immune therapy response, whereas persistence is a harbinger of progressing disease. This has tremendous treatment impact and benefit for your patients and also sparks the need for hereditary Lynch Syndrome testing with potential lifesaving impact for their families.



Case Study Prepared by Doctor Paul Walker  
Chief Medical Officer, Former Director of Thoracic Oncology at East Carolina University

Sources:  
- Nature Medicine  
- J Clin Oncol 37:1217-1227  
- J Natl Cancer Inst;2013;105:989-992  
- J Gastrointest Oncol 2020;11(4):826-828  
- N Engl J Med 2015;372:2509-20