Abstract: P1994

Title: IGH GENE REARRANGEMENT PATTERNS OBSERVED WITH THE USE OF FLUORESCENCE IN SITU HYBRIDIZATION (FISH) IN MULTIPLE MYELOMA PATIENTS

Abstract Type: e-Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

IGH translocations (trs) are highly important in multiple myeloma(MM) management. In real world, FISH analysis of *IGH* gene rearrangement(s) (GRA(s) begins with the application of*IGH* break apart probe (BAP) for the presence of *IGH* ts, and when found five main *IGH* partner genes (PGs), *FGFR3* (4p16.3), *CCND3* (6p21), *CCND1* (11q13), *MAF* (16q23), *MAFB* (20q12) are tested.

Aims:

IGH translocations (trs) are highly important in multiple myeloma (MM) management. In real world, FISH analysis of *IGH* gene rearrangement(s) (GRA(s) begins with the application of*IGH* break apart probe (BAP) for the presence of *IGH* ts, and when found five main *IGH* partner genes (PGs), *FGFR3* (4p16.3), *CCND3* (6p21), *CCND1* (11q13), *MAF* (16q23), *MAFB* (20q12) are tested.

Methods:

Mononuclear or CD138-enriched cells from bone marrow aspirates of 445 MM pts at the Moscow City Botkin Hospital during 2021-2023 years were used and tested by FISH for abnormalities of chromosomes 1(1p/1q), 5, 9, 13q, 15, 17p, 19, and presence of GRAs involving *IGH* and *MYC*. Next, cases with *IGH* GRAs detected by *IGH* BAP were evaluated for *IGH* ts with *FGFR3*, CCND3, *CCND1*, *MAF*, *MAFB* probes.

Results:

The *IGH* GRAs were seen in 239 (54%) pts, out of which: t(11;14) - 36%, t(4;14) - 20,5%, t(14;16) - 7,1%, t(6;14) - 4,6%, t(8;14) - 2,9%, t(14;20) - 1,3%. In 21.3%, the specific translocation partner (TP) was either not identified or the tr did not take place. In 6.3%, the evaluation of a TP was not attempted. The identified *IGH* GRAs were categorized based on their FISH *IGH* BAP signal patterns (SPs): \1) Typical tr (1Red(R),1Green(G),1Fusion(F) signals – 1R1G1F) SP was seen in 87 (36.4%) pts, with a tr involving one of five main PGs in 76 (87.4%) cases. The main PGs were *CCND1* (37.9%) and *FGFR3* (31.0%). In 11 cases the TP was not identified. \2) Atypical SP (2R1G1F, 1R2G1F, 1R1G2F, 4R1G1F, 2R1G2F, 3R2G2F, 2R2G2F) was seen in 22 (9.2%) pts, the main TP being the *CCND1*, and in one case a TP was not identified. \3) 5’ FISH probe deletion pattern (1R1F, 1R2F, 2R2F, 3R2F, 1R, 2R) was found in 79 (33.1%) pts, in 34 cases the *IGH* trs were detected. The main TP was the *CCND1*, and in 14 pts the PG identification was not attempted. \4) 3’ FISH probe deletion (1G1F, 1G2F) SP was seen in 4 (1.7%) pts, and in 3 such cases *IGH* trs were detected. The only TP observed was *FGFR3*.
\5) A combination of typical tr, atypical and deletion patterns (1R1G1F plus patterns listed in 2, 3, and 4) was found in 10 (4.2%) pts, and in 9 such cases IGH trs were detected, with *CCND1* (40%) and *FGFR3* (30%) being the most common TPs. \6) Pattern of red and green FISH signals without a fusion signal (1R1G, 2R1G, 2R2G, 1R3G, 3R2G, 4R4G, 3R1G) was observed in 35 (14.6%) pts, and in 28 cases IGH trs were detected, with *CCND1* (40%) and *FGFR3* (28.6%) being the most common TPs. \7) A partial 5’ IGH probe deletion pattern, i.e., a diminished green signal fused with one red signal in both fusion signals. The evaluation of a possible *IGH* tr was not attempted.

Summary/Conclusion:

In our experience, atypical *IGH* GRA patterns with *IGH* BAP are common in MM pts, so a cytogenetic analysis of 3’/5’ *IGH* deletions should include evaluation of specific TPs for the possible IGH trs as most pts demonstrate

the presence of IGH trs with a main PG in such cases. At the same time, it doesn't necessarily mean that if 3'/5' IGH deletions are observed the IGH tr did occur. owHA particular SP may also be indicative of specific *IGH* tr and assist in identification of a PG, as in cases with 3' *IGH* deletion where the single TP, the *FGFR3*, was identified.

Of interest is that in a few cases with atypical*IGH* BAP SPs, we identified t(4;14) and t(6;14) trs that coincided with previously detected *cMYC::IGH* t(8;14) tr, which might have important prognostic and therapeutic implications.

Keywords: Multiple myeloma