Data integration to identify a successful combinatorial therapy based on epigenetic drugs in a BPDCN xenograft model

Sequencing analyses

14 Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) patients (range 9-89 years, male:female ratio=10:4)

Patient-derived CAL-1 cell line

Data integration

- Whole-exome sequencing (WES)
- Sanger sequencing
- MiSeq Illumina technology
- Copy number variant (CNV) analysis
- RNA analysis
- Pathology tissue-chromatin immunoprecipitation (PAT-ChIP) sequencing

- The epigenetic regulatory program was the most significantly undermined (P<.0001)
- 25 epigenetic-modifiers were mutated (e.g., ASXL1, TET2, SUZ12, ARID1A, PHF2, CHD8)
- ASXL1 was the most frequently affected (28.6% of cases)

BPDCN xenograft mouse model

5.000 CAL-1 cells

110 NSG mice (6-8 weeks old)

Treatments	Median survival versus control	
Saline (control)	32 days	
Bortezomib	no beneficial	
5′- Azacytidine	43.6 days	(P < .01)
Romidepsin	no beneficial	
Decitabine	44.7 days	(P < .05)
Decitabine + Bortezomib		
Decitabine + Romidepsin	42.8 days	(P < .01)
Decitabine + 5′- Azacytidine	52.8 days	(P < .01)
Romidepsin + 5′- Azacytidine		
Romidepsin + Bortezomib		
Romidepsin + Bortezomib + Decitabine		
Romidepsin + 5′- Azacytidine + Decitabine	41.8 days	(P < .05)

◀ Best result in terms of survival

Sapienza *et al.*, Haematologica, 2019