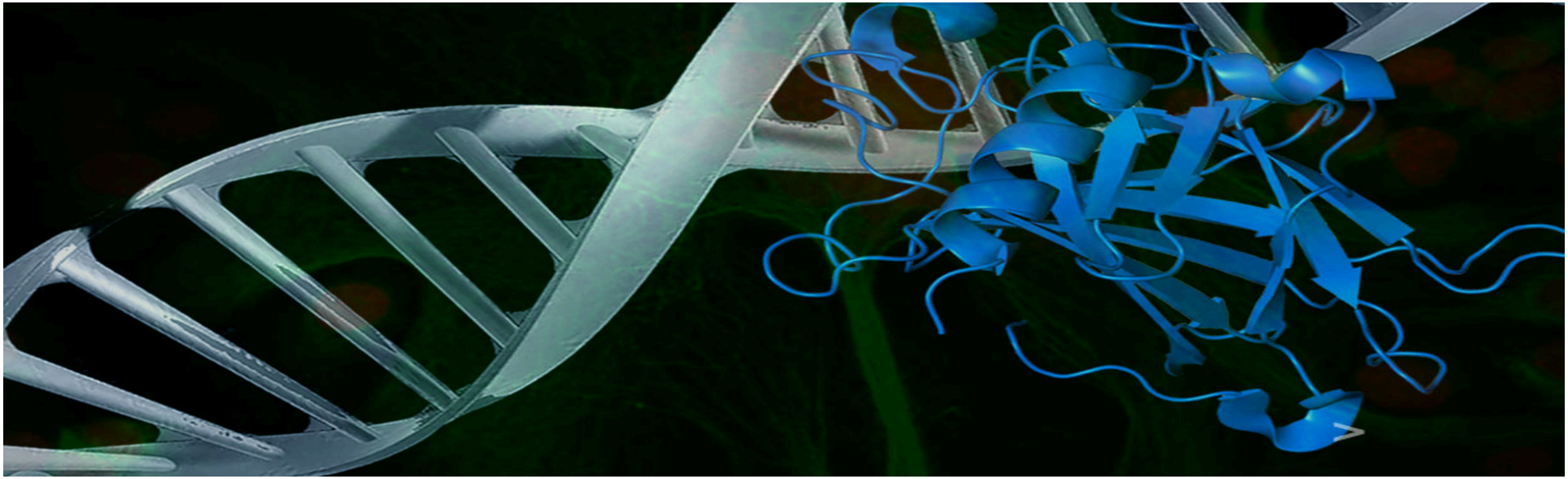


Recap and Update of Positive Data from Phase Ib/II Clinical Trials of APR-246 and Azacitidine (AZA) in Patients with *TP53* Mutant Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML) Presented at the 2019 American Society of Hematology (ASH) Annual Meeting in Orlando

December 12, 2019

Forward-Looking Statements

Certain information contained in this press release includes "forward-looking statements", within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, related to our clinical trials and regulatory submissions. We may, in some cases use terms such as "predicts," "believes," "potential," "continue," "anticipates," "estimates," "expects," "plans," "intends," "may," "could," "might," "likely," "will," "should" or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. Our forward-looking statements are based on current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties. Any or all of the forward-looking statements may turn out to be wrong or be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. These forward-looking statements are subject to risks and uncertainties including risks related to the success and timing of our clinical trials or other studies and the other risks set forth in our filings with the U.S. Securities and Exchange Commission, including our Quarterly Report on Form 10-Q. For all these reasons, actual results and developments could be materially different from those expressed in or implied by our forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this press release. We undertake no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.

APR-246 Combined with Azacitidine (AZA) in *TP53* Mutated Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML). a Phase 2 Study By the Groupe Francophone Des Myélodysplasies (GFM)

Thomas Cluzeau, Marie Sebert, Ramy Rahmé, Stefania Cuzzubbo, Anouk Walter-Petrich, Jacqueline Lehmann-Che, Isabelle Madelaine, Pierre Peterlin, Blandine Bève, Habiba Attalah, Fatiha Chermat, Elsa Miekoutima, Odile Beyne Rauzy, Christian Recher, Aspasia Stamatoullas, Lise Willems, Emmanuel Raffoux, Céline Berthon, Bruno Quesnel, Antoine F. Carpentier, David A. Sallman, Sylvie Chevret, Lionel Ades, Pierre Fenaux

Université Côte d'Azur , CHU of Nice, Hematology department; Mediterranean center of molecular medicine, INSERM U1065;

Groupe francophone des Myélodysplasies (GFM)

Baseline patient Characteristics

53 patients enrolled between Sept 2018 and July 2019

	Global cohort n=53	MDS n=34	AML n=19
Median age (range)	73 (44-87)	74 (46-87)	73 (48-94)
M/F	28/25	9/25	8/11
WHO 2016 classification			
MDS	65%	100%	*
Intermediate IPSS-R	6%	9%	*
High IPSS-R	6%	9%	*
Very High IPSS-R	53%	82%	*
AML	35%	*	100%
20-30% of blasts	24%	*	68%
> 30% of blasts	11%	*	32%
Cytogenetic risk			
Complex karyotype	87%	83%	88%
Monosomal karyotype	70%	50%	23%
Including del 5q	57%	33%	65%

Adverse Events of Interest

	All grade n=53	Grade 3/4* n=53
Febrile neutropenia	**19 (36%)**	**19 (36%)**
Neurological	**21 (40%)**	**3 (6%)**
Ataxia	13 (25%)	2 (4%)*
Cognitive impairment	4 (8%)	0
Acute confusion	4 (8%)	1 (2%)*
Isolated dizziness	3 (6%)	0
Facial paresthesia	1 (2%)	0

**grade 3 side effects seen in 2 patients with acute renal failure*

Neurological toxicity manageable:

- Full reversibility within 5 days of drug discontinuation
- No recurrence after dose reduction (one (13) or two (4) dose reduction)

Neurological toxicity related to:

- Lower glomerular filtration rate at treatment onset ($p<0.01$)
- Higher age ($p=0.05$)

Data on this slide has been updated: Please see next slide

Best Response according to WHO classification

in the 44 patients enrolled before June 2019

Intention to treat	MDS n=27	AML20-30 n=12	AML>30 n=5
ORR	**67%**	**50%**	**40%**
CR	59%	33%	0%
mCR/MLFS	4%	0%	20%
PR	0%	0%	0%
SD with HI	4%	17%	20%

*Evaluable patients**	MDS n=24	AML20-30 n=9	AML> 30 n=2
ORR	**74%**	**55%**	**50%**
CR	66%	44%	0%
mCR/MLFS	4%	0%	50%
PR	0%	0%	0%
SD with HI	4%	11%	0%

** ie patients who received at least 3 cycles and had a marrow evaluation after 3 cycles*

Data on this slide has been updated: Please see next slide

Updated Best Response according to WHO classification

- **In the 44 patients enrolled before June 2019**

Intention to treat	MDS n=27	AML20-30 n=12	AML>30 n=5
ORR	**63%**	**50%**	**40%**
CR	48%	33%	0%
mCR/MLFS	7%	0%	20%
PR	0%	0%	0%
SD with HI	7%	17%	20%

*Evaluable patients**	MDS n=24	AML20-30 n=9	AML> 30 n=2
ORR	**71%**	**55%**	**50%**
CR	54%	44%	0%
mCR/MLFS	8%	0%	50%
PR	0%	0%	0%
SD with HI	8%	11%	0%

- **Updated aggregate response rates#**

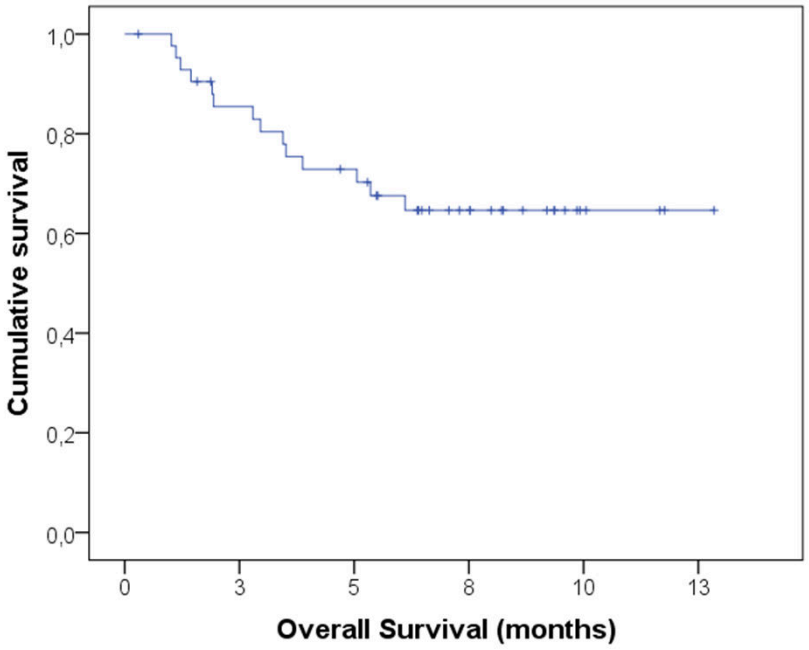
Intention to treat	MDS n=30#	AML20-30 n=12	AML>30 n=5
ORR	**67%**	**50%**	**40%**
CR	53%	33%	0%
mCR/MLFS	7%	0%	20%
PR	0%	0%	0%
SD with HI	7%	17%	20%

*Evaluable patients**	MDS n=27#	AML20-30 n=9	AML> 30 n=2
ORR	**74%**	**55%**	**50%**
CR	59%	44%	0%
mCR/MLFS	7%	0%	50%
PR	0%	0%	0%
SD with HI	7%	11%	0%

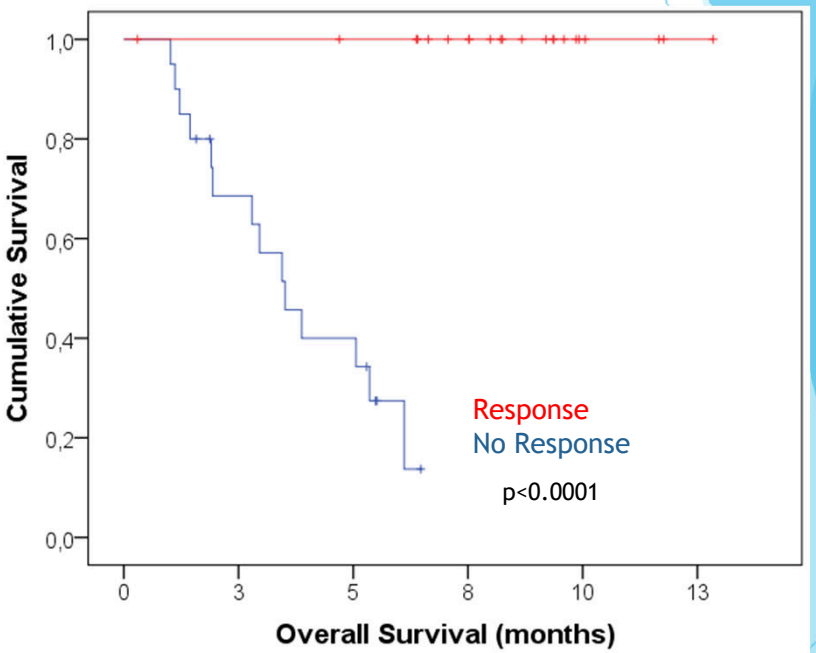
** patients who received at least 3 cycles and had a marrow evaluation after 3 cycles*

 # inclusive of 3 additional MDS patients who achieved CR

Overall Survival



Median FU: 6.4 months
Median OS: NR



Median FU: 6.4 months
Median OS in responders: NR
Median OS in non responders: 3 months

Phase 1b/2 Combination Study of APR-246 and Azacitidine (AZA) in Patients with *TP53* Mutant Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML)

David A. Sallman[1], Amy E. Dezern[2], Guillermo Garcia-Manero[3], David P. Steensma[4], Gail J. Roboz[5], Mikkael A. Sekeres[6], Thomas Cluzeau[7], Kendra Sweet[1], Amy McLemore[1], Kathy McGraw[1], John Puskas[1], Ling Zhang[1], Jiqiang Yao[8], Qianxing Mo[8], Lisa Nardelli[1], Najla H Al Ali[1], Eric Padron[1], Greg Korbel[9], Eyal C. Attar[9], Hagop M. Kantarjian[3], Jeffrey E. Lancet[1], Pierre Fenaux[10], Alan F. List[1], and Rami S. Komrokji[1]

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US Trial Baseline Characteristics

Cutoff: Nov 15, 2019

	All Patients (N=55)	MDS (N=40)	AML (N=11)	MDS-MPN / CMML (N=4)
Female, n (%)	29 (53)	17 (43)	8 (73)	4 (100)
Age in years, median (range)	66 (34 – 85)	66 (34 – 80)	68 (47 – 85)	57 (41 – 79)
Age Category, n (%)				
< 65	23 (42)	17 (43)	4 (36)	2 (50)
≥ 65	32 (58)	23 (57)	7 (64)	2 (50)
ECOG PS at treatment start, n (%)				
0	17 (31)	15 (37)	2 (18)	0 (0)
1	34 (62)	22 (55)	8 (73)	4 (100)
2	4 (7)	3 (8)	1 (9)	0 (0)
Disease type, n (%)				
MDS	40 (73)			
IPSS-R: Intermediate	4 (7)	4 (10)		
IPSS-R: High	8 (15)	8 (20)		
IPSS-R: Very high	28 (51)	28 (70)		
AML	11 (20)			
MDS-MPN / CMML	4 (7)			
Therapy-related, n (%)	18 (33)	14 (35)	4 (36)	0 (0)
Complex karyotype, n (%)	47 (85)	36 (90)	8 (73)	3 (75)
Transfusion dependence, n (%)	38 (69)	27 (68)	8 (73)	3 (75)

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AEs Regardless of Causality
Cutoff: Nov 15, 2019 (n=55)

Most common AEs (≥20% of patients)

Adverse Event, n (%)	Any Grade	Grade ≥ 3
Nausea	35 (64)	0 (0)
Vomiting	25 (45)	1 (2)
Fatigue	24 (44)	0 (0)
Constipation	23 (42)	0 (0)
Edema	21 (38)	2 (4)
Dizziness	20 (36)	1 (2)
Diarrhea	18 (33)	1 (2)
Febrile neutropenia	18 (33)	18 (33)
Peripheral sensory neuropathy	17 (31)	0 (0)
White blood cell decreased	17 (31)	16 (29)
Dyspnea	16 (29)	1 (2)
Headache	16 (29)	0 (0)
Lung infection	16 (29)	14 (25)
Neutrophil count decreased	16 (29)	16 (29)
Platelet count decreased	16 (29)	14 (25)
Cough	15 (27)	1 (2)
Pruritus	14 (25)	0 (0)
Anorexia	13 (24)	0 (0)
Ataxia / unsteady gait	13 (24)	2 (4)
Fever	12 (22)	1 (2)
Alanine aminotransferase increased	11 (20)	1 (2)
Mucositis oral	11 (20)	0 (0)
Tremor	11 (20)	1 (2)

Most common SAEs (≥5% of patients)

Serious Adverse Event, n (%)	
Febrile neutropenia	14 (25)
Lung infection	11 (20)
Respiratory failure	4 (7)
Sepsis	4 (7)
Dehydration	3 (5)

- Most common AEs related to APR-246 include gastrointestinal (nausea/vomiting) and neurologic
- 30 and 60 day mortality of 2% (n=1) and 5% (n=3), respectively.
- 3 patients (5%) discontinued secondary to adverse events (none secondary to APR-246 related AEs)

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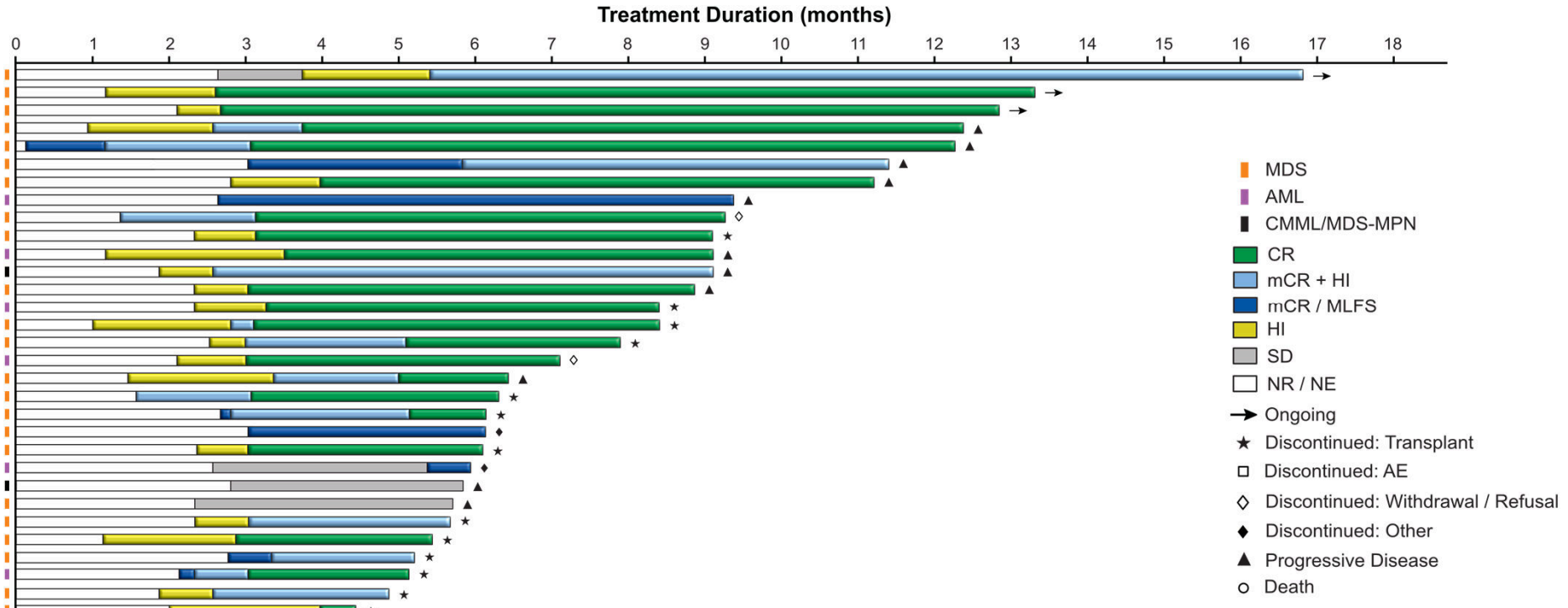
Response to Treatment in Evaluable Patients (N=45)

Cutoff: November 15, 2019



	Overall	MDS	AML	MDS-MPN + CMML
Evaluable patients, n	45	33	8	4
Overall response rate, n (%)	39 (87)	29 (88)	7 (88)	3 (75)
CR rate, n (%)	24 (53)	20 (61)	4 (50)	0 (0)
Duration of CR, months (median) [95% CI]	7.3 [5.8 – N.E.]	7.3 [5.8 – N.E.]	7.0 [3.3 – N.E.]	N.E.
Discontinued for transplant, n (%)	22 (49)	17 (52)	4 (50)	1 (25)

Median duration of follow-up = 10.8 months

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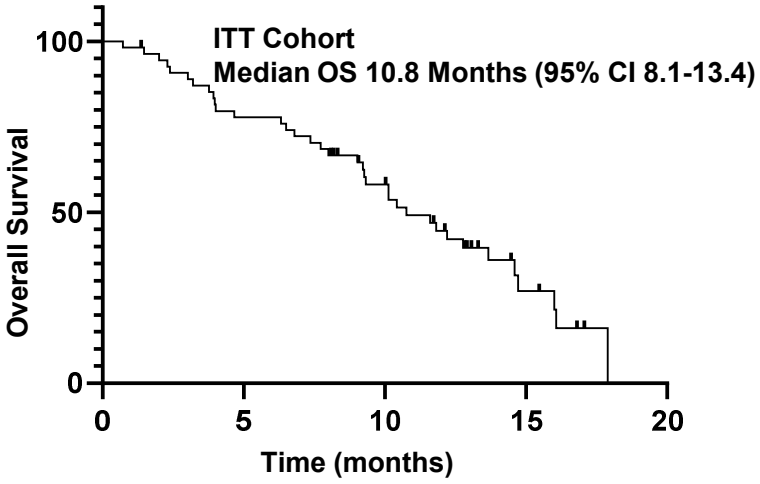
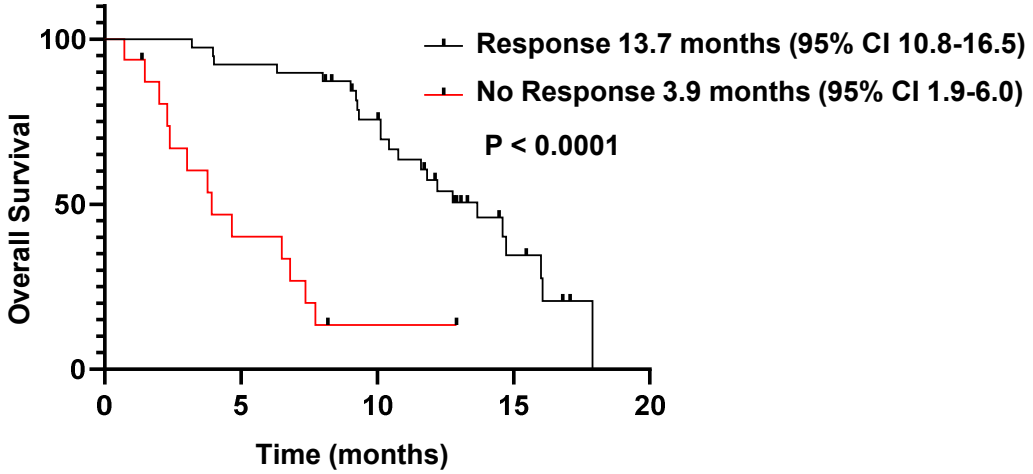
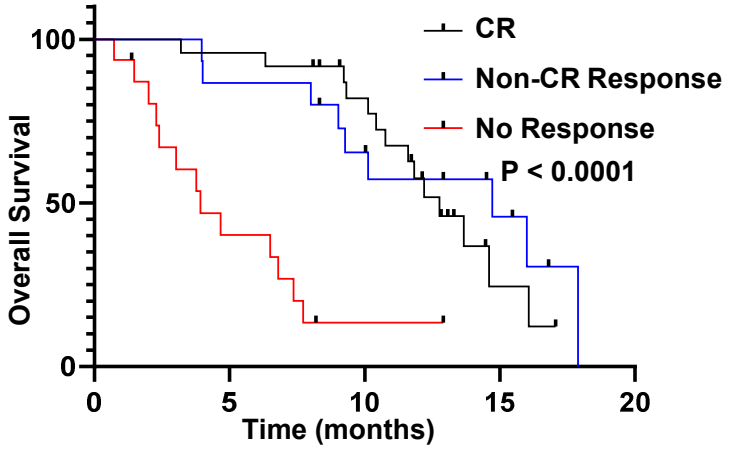
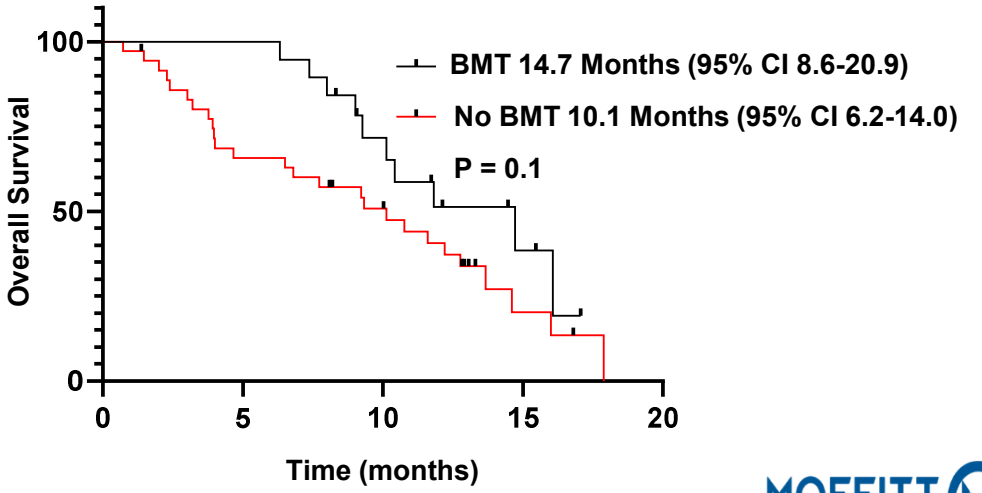
Survival

Cutoff: Nov 15, 2019









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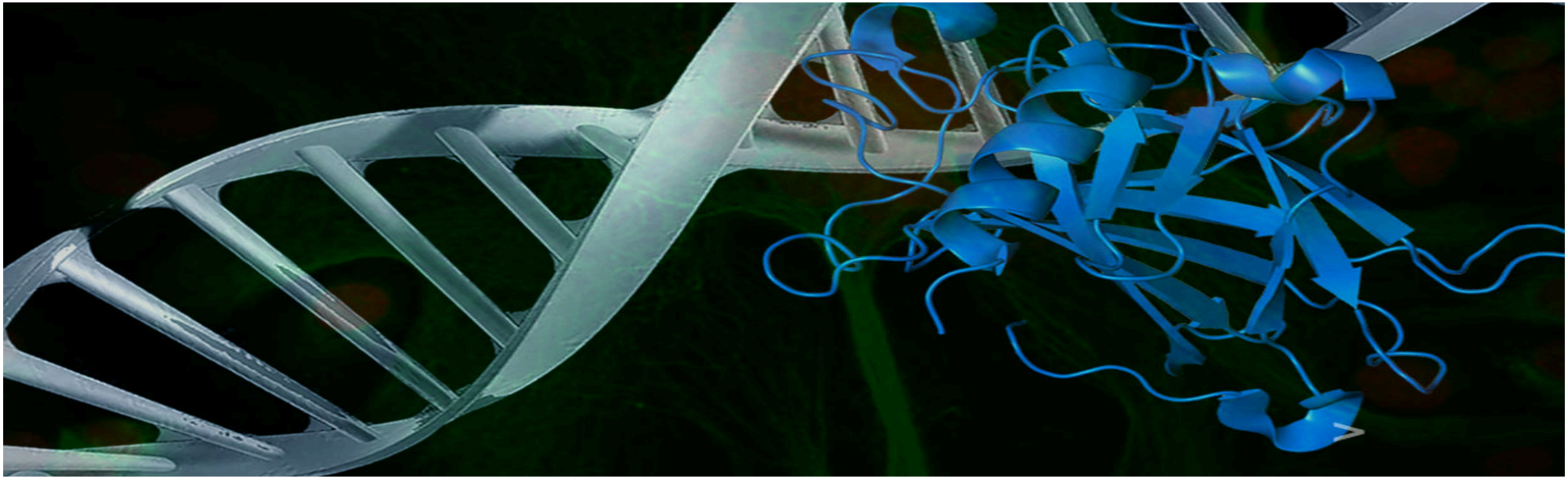
Summary

- **Highly concordant data from French and US Phase 1b/2 Trials in *TP53* mutant MDS/AML**
  - Encouraging response rate, response duration and survival in evaluable patients
    - 59-61% CR in MDS
    - 74-88% ORR in MDS
    - 52% rate of discontinuation for transplant in MDS patients in US trial
    - 8.4 months median duration of response in US trial
    - 7.3 months median duration of CR in US trial
    - 10.8 months overall median OS and13.7 months median OS in responding patients in US Trial
    - Median OS in responding patients not reached in French Trial – all responders still alive at the data cutoff

- **Other APR-246 Clinical Trials**
  - Pivotal Phase 3 MDS Trial
    - APR-246 + AZA for frontline treatment of *TP53* mutant MDS
    - Full enrollment in 1Q 2020 with final CR primary endpoint expected 2H 2020
  - Phase 2 MDS/AML Post-transplant Trial
    - APR-246 + AZA for post-SCT maintenance therapy of TP53 mutant MDS/AML
    - Full enrollment expected 1H 2020
  - Phase 1/2 AML Trial
    - APR-246 + Venetoclax ±AZA for treatment of relapsed/refractory AML
    - First patient enrollment expected Dec 2019



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