



# IACH

## VENETOCLAX AND POSACONAZOLE PLUS STANDARD DOSE CYTARABINE FOLLOWED BY ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR NEWLY DIAGNOSED ACUTE MYELOID LEUKEMIA

### Revolutionary Treatment of AML

Tran-Der Tan MD, Lun-Wei Chiou MD

Leukemia, Lymphoma, and Hematopoietic Stem Cell Transplantation Multidisciplinary Team  
Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

#### RATIONALE

The present standard treatment for ND AML is 3+7 (Daunorubicin or idarubicin x 3 days plus cytarabine x 7 days).

**Venetoclax plus azacytidine or low dose cytarabine** is effective for newly diagnosed unfit AML in VIALE A(1) and VIALE C trials(2), respectively, and allogeneic hematopoietic stem cell transplantation consolidation has been reported(3).

We choose **venetoclax 100 mg a day plus posaconazole 300 mg a day** PK of drug and economic consideration **and combined standard dose of cytarabine 100 mg/m<sup>2</sup>/d x 7 days** as the induction therapy.

#### Venetoclax Based Therapy

Venetoclax 100 mg plus posaconazole 300 mg daily and 7 days' cytarabine 100mg/m<sup>2</sup> in 7 patients and 4 patients received consolidation therapy with uninterrupted venetoclax plus posaconazole and 5 days' cytarabine 100 mg/m<sup>2</sup>/d.

Venetoclax 100mg plus posaconazole 300 mg daily and azacytidine 75 mg/m<sup>2</sup> for 7 days in one patient in induction and consolidation therapy.

#### RESULTS (I)

Eight patients have enrolled the treatment including 7 underwent venetoclax/posaconazole/cytarabine and one venetoclax/posaconazole/azacytidine patients.

Four patients were de novo AML and 4 were secondary AML (one myeloma, one MDS, and 2 breast cancer patients).

All patients were hematologic complete remission achieved in one month and 6 patients underwent allogeneic hematopoietic stem cell transplantation including one from matched sibling, two from matched unrelated, and three from haplo- identical donors (sons).

#### RESULTS (II)

Febrile neutropenia rates were similar to 3+7 treatment patients on historical comparison but shorter period of febrile illness.

**There was no grade II or higher adverse effect of oral mucosa and gastrointestinal tract as compared with conventional 3+7 therapy.**

Two out of six allo-transplant patients got leukemia relapse then salvage treatment ensued and CR2 achieved and the other 2 non-transplant and 4 allo-transplant patients are persisted in complete remission until this presentation.

#### CONCLUSION

1. Venetoclax based therapy is **feasible** and more **better tolerable** for all AML patients! Nearly no oropharyngitis or diarrhea as compared in 3+7 treatment. Most importantly, the **CR rate was 100%** (8/8) in our cohort.
2. **No man is fitted in front of 3+7 !!!!!**
3. **Post-venetoclax cytopenia** is to be concerned, however, continued venetoclax until remission achieved during induction therapy; once CR achieved, withhold or intermittent use of ventoclax is mandatory when severe cytopenia (neutropenia or thrombocytopenia) occurred during subsequent (consolidation) therapy.
4. **Post-venetoclax does not influence the neutrophil or platelet recovery after hematopoietic stem cell transplantation.**

#### REFERENCES

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2. Andrew H. Wei, Stephen A. Strickland Jr, Jing-Zhou Hou, et al. Venetoclax combined with low-dose cytarabine for previous untreated patients with acute myeloid leukemia: Results from a phase Ib/II study. J clin Oncol 2019; 37: 1277-1284.
3. K.S. Sandhu, S.Dadwal, D Yang, et al. Outcome of allogeneic hematopoietic cell transplantation after venetoclax and hypomethylating agent therapy for acute myeloid leukemia. <https://doi.org/10.1016/j.bbmt.2020.08.027>

Patient	1, 62Y/F	2, 55Y/M	3, 46Y/F	4, 62Y/F	5, 64Y/M	6, 65Y/M	7, 52Y/F	8, 59Y/F	Average
ANC < 500	26~30 days	18~10 days	21~10 days	0	12 days	89 days	22 days	30 days	19.89 days
ANC = 0	5~4 days	0~2 days	0~7 days	0	0	0	8 days	3 days	3.22 days
ANC >500 after end of C/T	+15~+36 days	+29~+17 days	+20~+18 days	0	+25 days	+84 days	+24 days	+19 days	22.56 days
Plt no transfusion after the end of C/T	+13 days~+11 months	+22~+32 days	+12~+23 days	0	+22 days	> 6 mnths	+17 days	+18 days	19.88 days
Transplant	N	Y (+16 & +12 days neu/plt engrafted)	Y (+16 & +9 days neu/plt engrafted)	Y (no transfusion)	Y (+21 & +5 days neu/plt engrafted)	N	Y (+19 & +14 days neu/plt engrafted)	Y (+20 & +13 days neu/plt engrafted)	18.4 vs 10.6 days

**CONTACT: Tran-Der Tan MD, [trander@kfsyscc.org](mailto:trander@kfsyscc.org)**

**[www.iachlive.cme-congresses.com](http://www.iachlive.cme-congresses.com)**