Abstract #285515

Effect of plinabulin, a Novel Late-Clinical Stage Immunotherapeutic Agent on the Adaptive and Innate Immune System.

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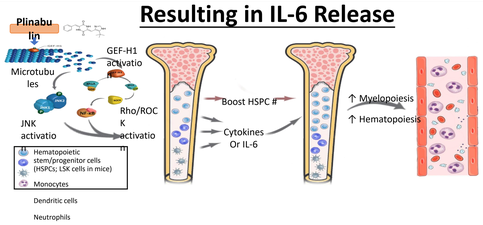
Plinabulin Overview

MoA - Plinabulin - first-in-class agent with GEF-H1 Release Resulting in IL-6 Release



Plinabulin (Plin) is a small molecule Dendritic Cell modulator, which in the presence of antigen, increases T-cell proliferation in an antigen-dependent manner marrow.

Plinabulin is a novel non-G-CSF small molecule, in development for the prevention of Chemotherapy-Induced Neutropenia (CIN) and is differentiated from Pegfilgrastim:

- ❖ Plinabulin has anticancer activity
- ❖ Plinabulin prevents chemotherapy-induced-neutropenia

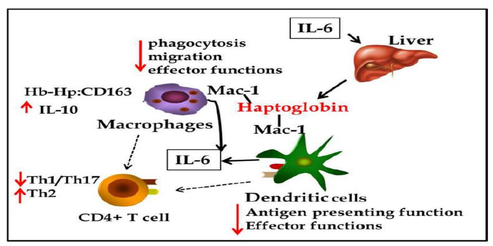
The addition of Plin to Docetaxel (Doc) improved mOS with 4.6 months vs Docetaxel monotherapy, and prolonged DoR with more than 1 year ($p < 0.05$), which is indicative of an immune-mediated mechanism of action (Mohanlal, ASCO-SITC 2017).

Neutrophils are our first line of **innate immune** defense against foreign invaders.

Here we analyzed the onset time of neutrophil increase following Plinabulin administration. In addition, we analyzed the impact of Plinabulin on plasma haptoglobin, which is an acute phase protein with anti-inflammatory effects together with immune-enhancing effects and is an integral part of innate immunity (Kristiansen Nature 2001).

Haptoglobin Effects on Innate Immunity is IL-6 Dependent

- **Plinabulin increases Tissue Levels of IL-6**



Galecea et Intechopen 2011

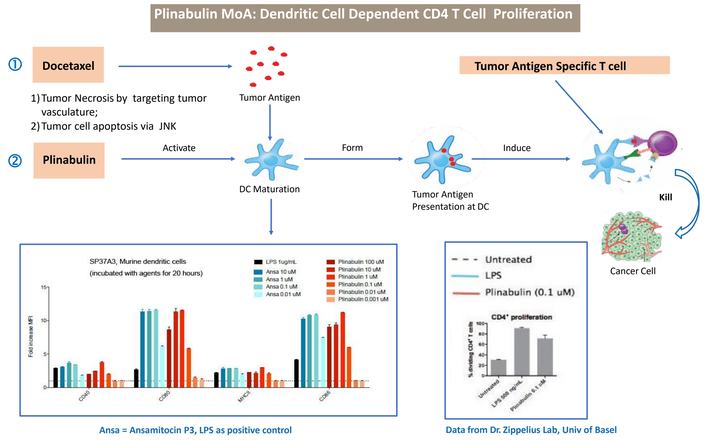
Plinabulin Development Pipeline

	Program	Indication	Trial name	Preclinical	Phase 1	Phase 2	Phase 3	Commercial rights	China NDA filing	U.S. NDA filing
Late stage	Plinabulin + docetaxel	NSCLC (2nd/3rd line)	Study 103		Phase 3 first interim data analysis completed			Global[1]	Q1 2020	2020
Late stage	Plinabulin	CIN	Study 105		Phase 3 primary end point met at interim analysis			Global[1]	Q1 2020	2020
Late stage	Plinabulin + pegfilgrastim	CIN	Study 106		Phase 2 efficacy / safety end points met			Global[1]	Q1 2020	2020
Investigator-initiated IO	Plinabulin + nivolumab	NSCLC (2nd/3rd line)	Fred Hutch/Univ. Washington/UCSD					Global[1]		
Investigator-initiated IO	Plinabulin + nivolumab + ipilimumab	SCLC	Rutgers University					Global[1]		
Investigator-initiated IO	Plinabulin + PD-1/PD-L1 + radiation/chemo	Various cancers (2nd/3rd line)	MD Anderson					Global[1]		

Note: [1] We own global rights to Plinabulin in all countries except China. In China, we currently own a 60% interest in our Chinese subsidiary, Dalian Wanchunbulin Pharmaceuticals Ltd. ("Wanchunbulin"), which owns a 100% interest in Plinabulin. Wanchunbulin has entered into definitive agreements for the sale of equity interests to certain investors, which are expected to close in the near term. Upon closing, it is expected that we would hold 57.14% of the equity interests in Wanchunbulin.

Plinabulin's Effects on the Adaptive Immune system

Plinabulin MoA: Dendritic Cell Dependent CD4 T Cell Proliferation



Ansa = Ansamitocin P3, LPS as positive control

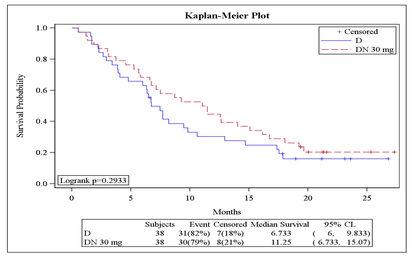
Data from Dr. Zippelius Lab, Univ of Basel

- Lloyd GK, Muller P, Kashyap A et al. Plinabulin: Evidence for an immune-mediated mechanism of action, AACR Tumor Microenvironment Event 2016

Plinabulin's Anti-Cancer Efficacy Results

Phase 2 OS Benefit in NSCLC Patients

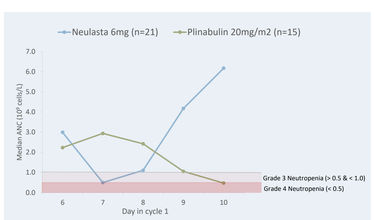
Durable Response and Extended Survival Benefit of 4.6 Month

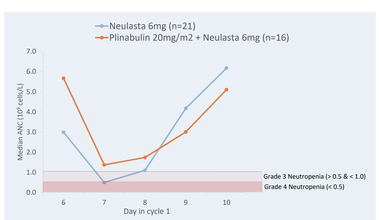


	Plinabulin / Docetaxel	Docetaxel alone
	N=38	N=38
mOS	11.3 M	6.7 M
	P = 0.29	
ORR	18.4 %	10.5%

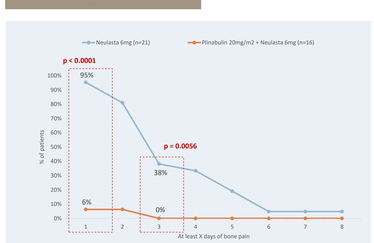
Plinabulin's Anti-CIN Efficacy Results

in Breast Cancer Patients receiving TAC chemotherapy





Reduced Bone Pain



Plinabulin Clinical Trial Effects

- **Anticancer Trial Effects:**
- **Better OS**
- **Better Safety**
- **Better QoL**

- **Anti CIN Trial Effects:**
- **Superior CIN effects vs Pegfilgrastim]**
- **No Bone Pain**

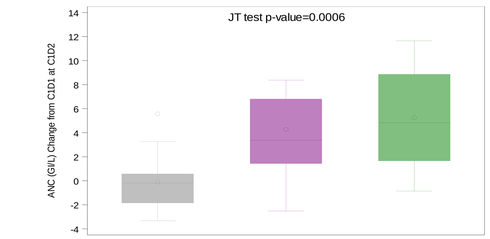
Plinabulin's Effects on the Innate Immune system

Absolute neutrophil count (ANC) and haptoglobin data were analyzed from Phase 2 study BPI-2358-106 (NCT03294577) with 10 (n = 15), 20 (n = 15) and 30 mg/m2 (n = 12) Plinabulin in Breast Cancer patients receiving TAC.
Plinabulin was administered on Day 1. ANC and Haptoglobin were analyzed by a Central Laboratory (Covance), from blood draws at predose, and post-dose Plinabulin at Day 2,3,6,7,8,9,10,11,12,13 and 15, and changes relative to predose value were evaluated.

- **Mean haptoglobin ($P < 0.0005$) and ANC ($P < 0.001$) levels increased with ~two-fold vs baseline levels.**
- **Plinabulin dose-dependently increased ANC within 1 day ($P < 0.001$) and Haptoglobin within 3 days ($P < 0.03$) of dosing.**
- **ANC levels remained increased for approximately 1 week and haptoglobin levels for > 3 weeks.**

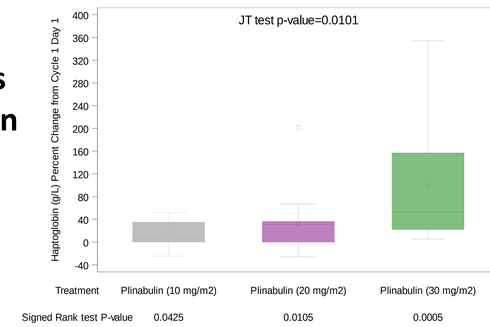
Plinabulin's Neutrophil Benefit

ANC change from C1D1 at C1D2



Plinabulin's Haptoglobin Benefit

Haptoglobin Percentage Change from C1D1



Conclusion

Plinabulin is a Potent Stimulator of the Adaptive and Innate Immune System

- **Plinabulin is currently in late-stage Phase 3 for:**
  - **NSCLC in 2nd and 3rd line**
  - **Chemotherapy-Induced Neutropenia (CIN)**

ASCO-SITC Clinical Immuno-Oncology Symposium — February 6–8, 2020 • Orlando, FL — #ImmunoOnc20

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