SM-88 efficacy and safety in metastatic breast cancers.

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Background:

SM-88 is a relatively non-toxic novel combination therapy (dysfunctional tyrosine, CYP3a4 inducer, mTOR inhibitor and oxidative stress catalyst) that has demonstrated efficacy in breast and other metastatic cancers. Early testing of SM-88 therapy with over 100 subjects has shown a potential efficacy signal, including RECIST responses in 13 different cancer types (JCO 2013, e22095), while maintaining a manageable toxicity profile (no grade 3-5 drug-related AEs). We assessed its effect in an updated cohort of breast cancer subjects.

Methods:

Retrospective chart review of metastatic breast cancer (mBC) subjects treated with SM-88 (aka SMK) under Phase I or compassionate use programs. All subjects received po SM-88 5 days/week. Combination therapy with other anti-neoplastics including parenteral SM-88, was used in 5 compassionate use cases.

Results:

A total of 25 mBC cases with 21 evaluable were identified from 107 charts of subjects treated with SM-88 between 2012–7. Mean age 51 (35 – 70); 95% white; median prior systemic therapies: 3 (1–8); and baseline ECOG: 1 (0 – 4). All subjects had previously treated progressing mBC and were considered incurable with 33% (7/21) refractory, 67% (14/21) recurrent. Overall response rate (ORR) was 43% (9/21) with responses seen across all receptor profiles (see table). Outcomes included improvement of ECOG

PS in 81% and 67% of EORTC QLQ-C30 “overall health" and “overall quality of life” plus pain reduction (NRS-11) in 57%. Subjects with 1 prior systemic therapy (n=7) had a median PFS of 9 months while those with >1 had a median PFS of 3.5 months. Metastatic locations were 62% (13/21) bone; 57% (12/21) liver/lung; 57% (12/21) lymph nodes. Clinical benefit and OS were no different with bone metastases (n=13) compared to without (median OS of 12 mo and 9 mo respectively). There were no unanticipated or drug-related adverse events.

Conclusions:

SM-88 has demonstrated potential efficacy in mBC with a favorable safety and QOL profile. There was no indication of cross-resistance based on hormone profile, prior treatments, or metastatic site.

	CR	PR	SD	Overall Disease Control	PFS mo	OS mo
ER+ and/or PR+ HER2- n= 12	25%	17%	33%	75%	5 (0 – 68)	10 (2 – 68)
TNBC n=5	0%	40%	40%	80%	12 (0 – 15)	12 (3 – 26)
HER2+ n=4	0%	50%	0%	50%	1 (0 – 6)	30 (7 – 70)