Journal of Biology and Medicine: Open Access

Short Communication | Vol 1 Iss 1

A Retrospective Review of 300 Case Reports, Quality of Life and Correlation With Biomarkers Related to Tumor Burden, in Advanced Cancer

M.A. Nezami[1*], Steven Hager DO[2], and Armin Chaychain[3]

[1]President and CEO, Sahel Oncology LLC, Orange Coast Medical Center of Hope Inc, Newport Beach, USA

[2]Medical Oncologist, California Cancer Associates for research and excellence (C Care), Fresno, CA, USA

[3]Research student, Sahel Oncology, USA

***Corresponding author:** Nezami MA, Sahel Oncology LLC, Orange Coast Medical Center of Hope Inc, Newport Beach, CA 92612, USA, Tel: 949-515-4673; E-mail: amnezami[AT]yahoo.com

Received: August 04, 2020; **Accepted:** August 20, 2020; **Published:** August 28, 2020

Abstract

It is currently the tumor size measured by RECIST criteria that is considered an indication for objective response to any effective therapy in cancer, however in advanced solid tumors, this indicator has been debated recently as it fails to correlate with clinical response, quality of life and even overall survival. In this short but large sample size case review, we look into a meaningful potential substitute for such metrics, defined by surrogates of tumor burden, and correlate that with biomarkers that can be easily measured through blood sample. We suggest further studies to be considered to validate our findings and propose a shift in current clinical practice by further generation of hypothesis, based on our review.

1. Background

Unresectable metastatic solid tumors is with rare exception, a fatal disease eventually. A few patients may enter a prolonged remission. However, for the majority of patients with metastatic disease, chemotherapy is administered with palliative intent to decrease tumor bulk, and prolong survival. That said the specific endpoints that best reflect benefit from systemic chemotherapy in metastatic disease remain unclear.

Objective response rates, as judged by a decrease in the size of measurable lesions, are increasingly considered to be poor surrogates for benefit in this family of cancers. The "disconnect" between objective tumor response and quality of life is particularly evident in studies of drugs such as molecularly targeted therapies.

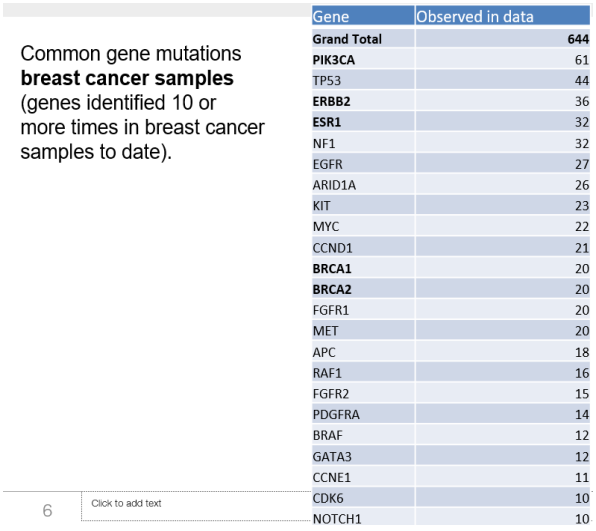
Increasing attention is being paid to other important indicators of clinical outcomes, such as reduced tumor burden, improved quality of life and disease stabilization. Stabilization of disease is increasingly viewed as a realistic endpoint

Citation: Nezami MA, Hager DOS, and Chaychain A. A retrospective review of 300 case reports, quality of life and correlation with biomarkers related to tumor burden, in advanced cancer. J Bio Med Open Access. 2020;1(1):109.

for metastatic disease [1-3]. Studies monitoring patients during treatment have shown that lower ctDNA dynamics correlate with better treatment response in colorectal ovarian, breast, non-small cell lung cancer (NSCLC), and melanoma [4-9].

2. Methods

We randomly selected and reviewed 300 cases treated solely or with an integration of supportive care with standard therapies through natural epigenetic therapy, aiming at reducing the metastatic tumor burden, measured by quality of life indicators as well as surrogate biomarkers such as circulating DNA, and circulating tumor cells. All patients started the program after educating them about their possible options of conventional and nonconventional treatments and consents obtained. The progression of disease was measures during or after the course of treatment through Tumor markers, growth factors, Imaging studies and markers for cancer growth, necrosis, LDH, circulating DNA and Circulatory tumor cells (CTC). In this review particularly the circulating DNA was randomly selected as biomarkers of tumor burden. The Fig. 1, manifests the most common findings in breast cancer cases, as an example. Fig. 2. manifests the cancer type category of the samples examined on April 2019.



Gene	Observed in data
Grand Total	**644**
PIK3CA	61
TP53	44
ERBB2	36
ESR1	32
NF1	32
EGFR	27
ARID1A	26
KIT	23
MYC	22
CCND1	21
BRCA1	20
BRCA2	20
FGFR1	20
MET	20
APC	18
RAF1	16
FGFR2	15
PDGFRA	14
BRAF	12
GATA3	12
CCNE1	11
CDK6	10
NOTCH1	10

Fig. 1. Manifests the most common findings in breast cancer cases, as an example.

Treatment consisted of multitargeted epigenetic therapy (MTET) in a patented protocol which consists intravenous application of off label natural histone deacetylase inhibitors and demethylators.

Patients were 21 to 83 years old, with mixed ethnicities and backgrounds. More than ¾ of the patients had received and exhausted prior traditional care. The minimum treatment course was two weeks and patients data were followed up to 10 years post therapy, when available (2010-2020).

3. Results

There were statistically significant positive changes in performance scales of patients with advanced disease by integration of the palliative and supportive care. In the first two weeks post initiation of the therapy, there was in

average 1.3point improvement in ECOG scoring. We also observed reduced hospitalizations and associated morbidities compared to historical data, as control. This finding was associated with a positive desirable change in biomarkers, defined by liquid biopsy. The circulating tumor cell analysis confirmed 85 percent reduction of mRNA expressions of all EpCAM markers, indicated by the lab (Biofocus Lab) Telomerase, ERBB2, c Myc, and CK 19/20. This reduction was noticed in average after 10 treatments.

Samples to date by cancer type, through end of April, 2019

*Definitions on following slide

Cancer Category	Count of samples
BLADDER	7
BONE / SOFT TISSUE	14
BREAST	186
CERVIX	5
ENDOMETRIAL/Uterine	11
GI	59
HEAD NECK	16
KIDNEY	7
LUNG	34
PROSTATE	50
Misc/Other*	42
OVARIAN	34
SKIN	26
Grand Total	**491**

Fig. 2. Manifests the cancer type category of the samples examined on April 2019**.**

4. Conclusions

We conclude that objective antitumor response defined by tumor size, may not necessarily reflect the best end point for clinical response. As such successful therapeutics could still improve clinical outcome by reducing tumor metastatic burden and improving quality of life. We suggest that further studies be conducted to prove the concept and development of novel epigenetic therapies aimed at reducing metastatic burden and quality of life in advanced solid tumors, and further integrated in the therapeutic approach to patients with advanced disease.

REFERENCES

1. Ooki A, Morita S, Iwamoto S, et al. Patient-reported symptom burden as a prognostic factor in treatment with first-line cetuximab plus chemotherapy for unresectable metastatic colorectal cancer: Results of Phase II QUACK trial. Cancer Med. 2020;9(5):1779-1789.
2. Geiger C, Chen Z, Zhang C, et al. Investigating the correlation between disease burden and symptoms in patients with advanced stage lung cancer. J Clin Oncol. 2015;33(15):doi:10.1200/jco.2015.33.
3. Merker VL, Bredella MA, Cai W, et al. Relationship between whole-body tumor burden, clinical phenotype, and quality of life in patients with neurofibromatosis. Am J Med Genet A. 2014;164A(6):1431-1437.
4. Elshimali Y, Khaddour H, Sarkissyan M, et al. The clinical utilization of circulating cell free DNA (CCFDNA) in blood of cancer patients. Int J Mol Sci. 2013;14:18925–18958.
5. Bettegowda C, Sausen M, Leary RJ, et al. Detection of circulating tumor DNA in early- and late-stage human malignancies. Sci Transl Med. 2014;6(224):224ra24.
6. Bardelli A, Pantel K. Liquid biopsies, what we do not know (yet). Cancer Cell. 2017;31(2):172–179.
7. Diehl F, Schmidt K, Choti MA, et al. Circulating mutant DNA to assess tumor dynamics. Nat Med. 2008;14:985–990.

8. Forshew T, Murtaza M, Parkinson C, et al. Non-invasive identification and monitoring of cancer mutations by targeted deep sequencing of plasma DNA. Sci Transl Med. 2012;4(136):136ra68.
9. Newman AM, Bratman SV, To J, et al. An ultrasensitive method for quantitating circulating tumor DNA with broad patient coverage. Nat Med. 2014;20:548–554.

Citation: Nezami MA, Hager DOS, and Chaychain A. A retrospective review of 300 case reports, quality of life and correlation with biomarkers related to tumor burden, in advanced cancer. J Bio Med Open Access. 2020;1(1):109.