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The Plasma Kinetic of Tumor Biomarkers: Experience of the Oran EHU

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Abstract

The success of therapeutic control of tumor processes depends on their early diagnosis. It is therefore necessary to develop both reliable and simple methods for identifying tumors from the early stages of evolution. This demand is at the basis of the development of biological markers of cancer called tumor markers (TM) [2,10,11]. The range of measurable tumor markers expand day by day, although some of them are not discriminative of a benign or malignant process, their utility remains considerable in the assessment of therapeutic effect and the surveillance of the disease evolution after treatment [10,8,11,12].

The Interpretation of the serum levels of TM is based on the kinetics' notion is more sensitive and relevant than that based on the static threshold [5,9,11], the later value of which is neither adapted to the nature of the treatment nor the precocity of the signal even the assay reagents used as well.

Within this study, "CHADOU TUMOR MARKER KINETIC" or CHA-TM KINETIC software was developed by Dr H. CHADOU. It allows automatically plotting the tumor marker evolution curves within time function [3, 10, 11], as well as the calculation of the biological parameters associated with each marker (initial concentration, apparent half-life [7,8,11], nadir, doubling time) [1,4,8,410,11,12].

The objective of this work is to demonstrate, through a case study, the importance of this software in the management of patients with different cancers such as breast, ovarian cancer and digestive cancers, at the University Hospital 1st November 1954 - ORAN (EHUO)

Keywords: Cha-Tm Kinetic Software, Tumor Markers, Kinetics, Half-Life, Nadir, Doubling Time

Introduction:

The success of therapeutic control of tumor processes depends on their early diagnosis. It is therefore necessary to develop both reliable and simple methods for identifying tumors from the early stages of evolution.

This demand is at the basis of the development of biological markers of cancer called tumor markers (TM) [2,10,11]. By increasing the specificity of cancer exploration, tumor markers allow better prescribing of radiological examinations provided that there is a reliable discrimination threshold for the diagnosis and detection of metastatic disease.

At all levels, it requires accurate determination of serum marker levels.

The use of tumor markers remains essential in the detection and following of the disease evolution [8, 11,12].

However, the interpretation of these serum levels based on a single value does not make it possible to evaluate either the efficacy of the treatments or the resistance of the tumor [4,5,9,10,11], henceforth the benefit of the use of a relevant method based on the "Study of the kinetics of the tumor markers [5,10,11] which makes it possible to ensure both a maximum of therapeutic efficacy and a minimum biological reagents use and the cancer chemotherapy whose cost remains very expensive.

Nevertheless, it requires a software that enable of the integration of the clinical and therapeutic data and allow for a graphical representation [3,4,10,11] of the kinetics and calculate the various kinetic parameters[10].

In this context, "CHADOU TUMOR MARKER KINETIC "or CHA-TM KINETIC software was developed by Dr.CHADOU.H (resident in pharmacology in Pharmacovigilance Department of

University Hospital Establishment at Oran UHEO and Research laboratory in pharmaceutical development (RLPD).

This software allows the graphic representation of the tumor markers kinetics (CA 125, CA19.9, CA 15-3, PSA, ACE, AFP, HCG, ...), the post -op or post-therapeutic following and the calculation of the different parameters (initial concentration, apparent half-life time [7,8,11], nadir, doubling time) [1,4,8,11,12] to a better evaluation for the therapeutic efficacy of anticancer drugs [5,8] and management of patients with different cancers such as Breast, ovary, prostate and colon cancer.

Patients and methods:

At present, we received 26 patients, 19 women and 7 men, aged between 37 and 77, with an average of 57 years. Carriers of different types of cancers: 10 patients with breast cancer, 4 have ovarian cancer and 12 patients with digestive cancers (Rectum, pancreas, gallbladder and colon), 8 of which are in the metastasis stage (hepatic, Pulmonary, bone and cerebral). (Fig. 01, 02, 03).

The quantitative determinations of serum concentration of tumor markers: CA 19-9 (52%), CA 125 (14%) and CA 15-3 (34%) is realized by immunoassay [12] whose use micro-particle immunoassay technology by chemiluminescence CMIA in the

Architect TM Abbott analyzer, with flexible dosing protocols called chemiflex.

Figure 01: Patients distribution by Sex.

Figure 02 : Patients distribution by cancer variety.

Figure 03 : Patients distribution by measured tumor marker.

The results are processed using the CH-TM KINETIC software whose allows the graphic representation of the evolution of markers serum concentrations within time function for all patients with secreting tumors.

The graph is plotted in semi-logarithmic coordinates with a logarithmic-scale concentration axis and arithmetic scale time axis. (Figure04)

The curve analysis and the calculation of parameters the can be done after the third point.

Also, it requires a regularly dosages according to a program established whose depend to the treatment protocol, an access to the patient's file in order to have clinical and biological data.

Results:

The graphic representation of the evolution of serum concentrations of tumor marker within time function for all patients with secreting tumors [5].

The mathematical analysis allows to calculate various biological parameters which are a powerful indicator of therapeutic efficacy and relapse risk: its is the initial concentration, the apparent half-life of the marker, the type of model (mono or bi exponential) [4,5], nadir and its corresponding time. In the kinetic approach, each patient represents his own control and any new serum concentration of tumor marker is interpreted according to the previous value.

The patient results are given as soon as possible in PDF (ready for printing) (Figure 04).

Discussion:

The tumor markers whose the essential indication is the post-therapeutic following of the tumors is a simple, inexpensive and very reliable examination when used judiciously.

By making each patient his own referent, the kinetic approach makes it possible to get rid of interindividual variability.

So, this approach of anticancer therapy individualization is very informative than an absolute value of the latter because it allows to define the different indicators of therapeutic efficacy and relapse risks.

The half-life: represents the necessary time to obtain the half of the serum concentration of tumor marker calculated in the initial phase [11].

It provides information about the efficacy of cancer therapy and the sensitivity to chemotherapy and / or radiotherapy [4]; This the half-life makes it possible to appreciate the quality of the excision during an operation.

The nadir: is the minimum concentration measured under treatment or after treatment: it is an indicator of residual disease [4,11].

The doubling time: represents the necessary time to doubling the tumor marker serum concentration [11] and therefore the number of tumor cells.

It provides information about the aggressiveness of the tumor [2,4] and the metastasis risks.

The interpretation of the marker serum level must take into

consideration its profile evolution, clinical and radiological context.

The report incorporates the evolution of the individual tumor marker kinetics, the clinical history of patient and the apparent biological value of the marker in order to help the clinician in his healthcare procedure.

Case study:

This example demonstrates the importance of CHA-TM KINETIC software in the following of cancer evolution.

71-year-old Patient named S.G. with gallbladder cancer T2NxMx stage diagnosed since October 2012.

Figure 05 : Semi logarithmic curve of the kinetics of CA 19-9 realized by the CHA-KINETIC software

The patient received the following chemotherapy:

Day 0 (N1): protocol GEMZAR.

(N1 - N3): the same protocol GEMZAR. (N1 -N2) Slow regression (long half-life) that exhibit the resistance to treatments.

(N2 -N3): relapse.

(N4 - N5): changement of the protocol GEMZAR to GEMOX (gemcitabine + oxaliplatin): quick Regression (short half-life) which means that the later Protocol is very effective.

Without CHA-TM KINETIC software and owing to the regression of CA19-9 serum concentrations, the clinician hadn't change the protocol of anti-cancer chemotherapy til relapse (N3).

However, this problem is avoidable if he changed the protocol when the CHA-TM KINETIC software indicated the presence of the resistance to the initiated treatment (long half-life between N1 and N2). This software permits to evaluate the efficacy of the ant-

cancer chemotherapy and the resistance of the tumor as well as the prevention of metastasis risks.

Conclusion:

By increasing the specificity of cancer exploration, the tumor markers allow a better prescription of the radiological examinations provided that reliable discrimination threshold is available for the diagnosis and the detection of the metastatic disease.

For this, the use of the kinetic of the tumor markers to follow the evolution of cancers has been essential.

Generally, this tool allows to integrate the studies of the plan of cancer in Algeria in the field of the rationalization of the expenses of the health and the management of the cancer.

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