

Report on the results obtained from the pilot project “INTEGRATED MEDICINE TO IMPROVE THE QUALITY OF LIFE OF CANCER PATIENTS” conducted at the Andrea Gallino Hospital from January to December 2017

Introduction

The aim of integrated medicine is to treat patients in their entirety in order to enhance their physical, psychological, moral, and social wellbeing. It offers patients everything that the most advanced orthodox medicine has to offer, combined with the holistic perspective of complementary medicine. The result is a medicine focused on the individual, capable of reducing the side effects of therapies, and allowing patients to actively participate in their health process.

“Rational” medicine dates back to Hippocrates (IV century BC) and originated as holistic medicine. Hippocrates thought that treatment should be focused on the individual rather than the disease. This was in contrast with the rival Cnidus school, which adopted a reductionist conception similar to the contemporary medical approach. Volker Diehl was among the first in Europe to propose the term “integrated medicine”, and he explained in detail the reasoning and motivations that led him to embrace it in his review article (1). It should be remembered that Volker Diehl was one of the leading modern researchers into pathogenesis and the treatment of Hodgkin's disease.

Aims of the study (SF36 questionnaire)

The main aims of our study were to improve the quality of life and wellbeing of patients. The study was based on assessment using the SF36 questionnaire. This instrument gives a multidimensional assessment of the quality of life correlated to the state of health. The questionnaire measures eight “domains” associated with health: physical state, role correlated with physical state, pain, vitality, general state of health, role correlated with emotional state, social relations, and mental health. These parameters are quantified from 0 to 100 and the lower the score the higher the disability and the worse the perceived quality of life. The results of the questionnaire reveal different aspects of the patient's state of health: three parameters regard physical health (physical activity, limitations to physical role, pain), two regard health in general (general health and vitality), and three regard psycho-emotional health (social activity, limitations to emotional role, mental health). The authors believed that this questionnaire could fully express the potential impact of integrated medicine on the perceived wellbeing and quality of life of patients and the resulting data was subjected to statistical analyses. Table 1 lists the definitions of the individual domains of the SF36 questionnaire.

Table 1 Meaning of the SF-36 questionnaire scores

Domain	N. items	negative extreme (0)	positive extreme (100)
physical activity (AF)	10	Marked limitation to physical activity including personal hygiene due to the disease	Conducts all types of physical activity including the most vigorous without limitations caused by the disease
limitations to physical role (LAF)	4	Problems with work or other daily activities due to physical health	No problems with work or other daily activities due to physical health
physical pain (DF)	2	Very intense and extremely limiting pain	No pain or limitations due to pain
general health (SG)	5	Assessment of personal health as bad and fear of possible deterioration	Assessment of general health as excellent
vitality (V)	4	Feeling tired and exhausted all the time	Feeling in good spirits and energetic all the time
social activities (AS)	2	Serious frequent interference with normal social activities due to physical and emotional problems	Conducts normal social activities without interference from physical or emotional problems
limitations to emotional role (LAE)	3	Difficulty with work or other daily activities due to emotional problems	No difficulty with work or other daily activities due to emotional problems
mental health (SM)	5	Constant feeling of nervousness or depression	Feeling constantly at peace, happy, and calm

Previous experience

In January 2014 our clinic introduced integrated medicine for patients with chronic debilitating immune-mediated diseases classified as rare. It was believed that integrated medicine might be particularly beneficial for these patients because they almost always experience an unsatisfactory quality of life for a variety of different reasons. The complexity of the clinical picture slows down diagnosis and is associated with a psychological malaise caused by the patients' uncertainty about their future. There are often relational difficulties with doctors and family, who in the absence of a definite diagnosis tend to blame patients for their condition of "infirmity", which is interpreted as hypochondriacal. Even when a diagnosis is established, the patients' difficulties persist due to the lack of resolute treatments free of toxicity. Patients are typically relatively young with chronic highly debilitating diseases that radically impact their quality of life and sense of personal value, generating problems in personal interaction and social relationships. For sixty-eight of these patients, orthodox medical treatments were

associated with complementary medical supports including: ion resonance sessions, acupuncture, homeopathy, homotoxicology, shiatsu, psychotherapy, life-coaching, and hypnosis in individual and group sessions, as well as an antioxidant/anti-inflammatory diet. In the majority of these patients, benefits were achieved in the progression of the disease and their psycho-physical wellbeing. An increase in physical activity was also observed along with a reduction in numbers and dosages of pharmaceutical drugs, an improvement in familial relations, and better social interaction. All eight domains of the SF36 questionnaire exhibited a statistically significant improvement over the course of treatment (2).

Rationale of the study

A series of scientific studies have revealed the value of integrated medicine for patients affected by neoplastic pathologies, not only for the improvement of quality of life, but also under the economic profile of health costs (3-5). Furthermore, it has been demonstrated how the quality of life of these patients is statistically correlated to their survival (6-8).

We offered patients the following complementary medical supports: administration of, impedance personalized, extremely low intensity and low frequency electromagnetic fields (ion resonance treatments), acupuncture, shiatsu, individual and group psychological support, personalized diet, music therapy, and yoga. The choice of supports was guided by the need to provide therapies that were antioxidant (diet and ion resonance), anti-inflammatory/analgesic (acupuncture, ion resonance, shiatsu, diet), relaxing and psycho-balancing (psychological support, shiatsu, music therapy, yoga, ion resonance, acupuncture), with the overall aim of positively affecting the physical and mental health of the patients.

Numerous studies have demonstrated that diet can play a fundamental antioxidant role through the use of nutraceuticals and special dietary regimes, providing an important preventive and protective antineoplastic action (9,10). Anti-oxidant and nutraceutical diets stimulate the Nrf2 transduction factor, with reduced production of pro-inflammatory cytokines and protective effects on the organism (11).

The activation of the Nrf2 transduction factor is also achieved by ion resonance treatment (12), which induces an anti-oxidant effect (13), anti-inflammatory/analgesic effect (14), and myeloprotective effect (15). It is also known that ion resonance is beneficial for the psycho-emotional sphere, since it promotes an increase in electroencephalographic alpha waves, understood to be associated with a state of relaxation (16).

The positive effects of acupuncture on patients under chemotherapy treatments and those suffering pain over the course of neoplasia are presented in reviews (17-19). Likewise, the effects of shiatsu manipulations and massage, music therapy, and yoga are reported in reviews cited above (3-5). As regards the benefits of psychological support for cancer patients, the evidence reported in international scientific literature is overwhelming (20-22).

Materials and methods

We offered the following treatments:

- 1) administration of impedance personalized extremely low intensity and low frequency electromagnetic fields (ion resonance treatments) with the medical device SEQEX (S.I.S.T.E.M.I. srl – Pergine Valsugana (TN)) twice a week for at least three months. SEQEX is an electromedical device which produces 30 different

shapes of electromagnetic waves with intensities between 1 to 100 μT and a frequency between 1 to 100 Hz (Extremely Low frequency ElectroMagnetic Fields [ELF-EMF]). In the first session (test-phase) for each patient, the shape, intensity and frequency of waves were selected on the basis of the impedance, tested in the body of the subject during the test phase. In fact, the body of the tested subject responds to each singular impulse received with a cellular ionic movement (endogenous cyclotron ion resonance) and the cellular response was measured by changes in body impedance. The waves that produce better ionic movement were selected and saved in a memory card. Successively (treatment-phase) the patients were treated with ELF-EMF using the waves selected and stored digitally on his/her own card. After 8 treatments, the test-phase was repeated.

- 2) Acupuncture was administered once a week for at least three months.
- 3) Shiatsu was administered once a week for at least three months.
- 4) Individual and group psychological support was offered on the base of emotional needs.
- 5) Personalized diet was offered to obtain a reduction of oxidative stress and of side effects of chemotherapy.
- 6) Music therapy (active and receptive music therapy techniques, sound relaxation techniques) was offered once a week for two-three months.
- 7) Yoga was offered once a week for at least three months.

All the patients had treatment with ELF EMF, 75% had acupuncture, 68% had Shiatsu, 50% had psychological support, 70% had personalized diet and 50% had Music therapy and yoga

Characteristics of patients

The study included 100 patients, 27 males and 73 females, all resident in the Liguria Region, average age 58 years (from 31 to 92). The oncological diseases included the following tumors: cerebral 4, sarcoma 3, lymphoma, K-ras gastro-enteric 7, K-ras mammary 36, K-ras ovarian 9, K-ras pulmonary 7, K-ras pancreatic 5, K-ras laryngeal 2, K-ras renal 1, K-ras endometrial 1, leukemia 2, Waldstrom's macroglobulinemia 2, mesothelioma 2, melanoma 2. The patients were referred from six oncology and hemato-oncology clinics in the Genoa region (IRCS San Martino Hospital, Galliera Hospital, Gallino Hospital, Micone Hospital, Villa Scassi Hospital) and three Milan hospitals (Humanitas, European Oncology Institute, and San Raffaele Hospital). Of the 100 patients treated under the therapeutic protocol, six patients abandoned treatment early, and nine were initiated during the months of November and December and consequently have not yet completed the first three-month follow-up. Ten of the patients included in the study were under treatment for a second tumor, with nine cases of metachronous tumor and one synchronous tumor. At the time of neoplasia diagnosis, six patients were under treatment for an immuno-mediated disease (vasculitis, APS or antiphospholipid antibody syndrome, Sjogren's syndrome, undifferentiated connective tissue disease, Churg Strauss syndrome, and dermatomyositis). These were therefore complicated patients, already physically and psychologically undermined by the previous neoplastic diseases or by the associated chronic diseases.

Attachment 1 provides the demographic details and clinical characteristics of all the patients included in the study. Figure 1 presents a graph of the referring Oncological Clinics in order to underline that all the major Oncology Departments of Genoa province sent patients to take part in the integrated medicine program, along with three Milan Oncology clinics who referred patients under their care but resident in the province of Liguria.

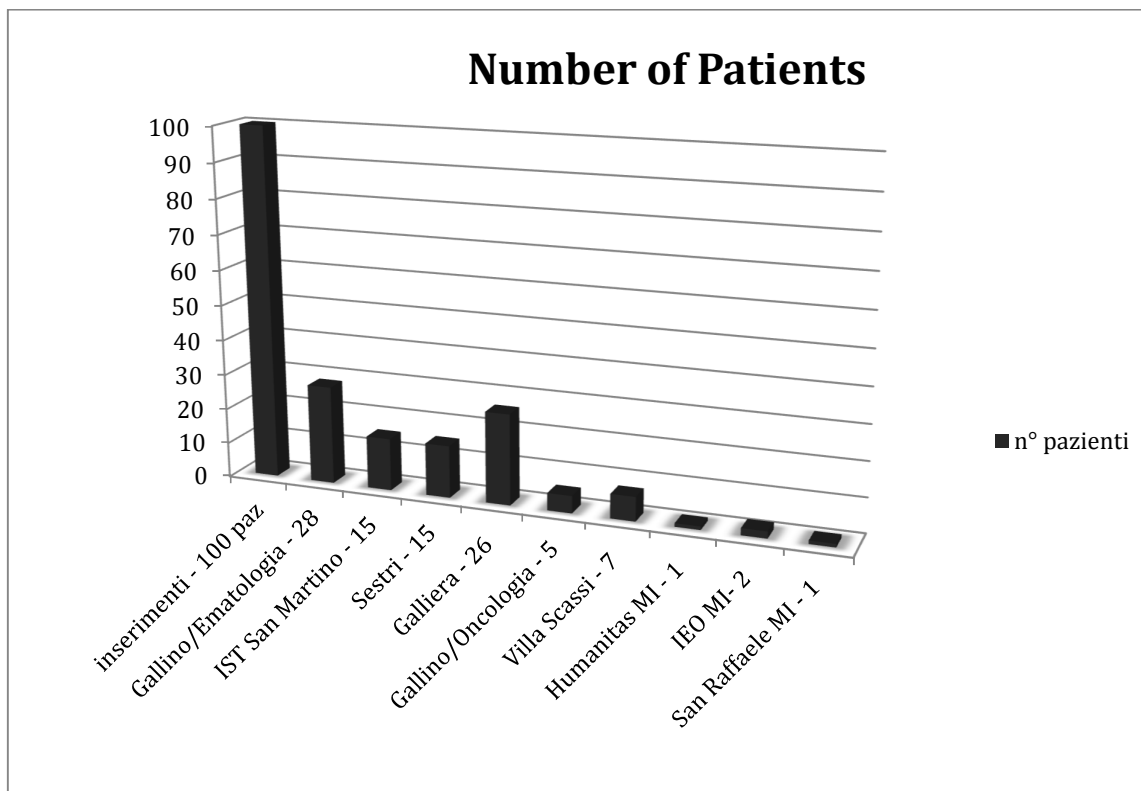


Figure 1. Oncological Clinics that collaborated in the study and number of patients referred from each one.

Results

Table 2 shows the results achieved for the perceived quality of life and wellbeing of the patients over the course of the study. The table indicates the medians for all the values recorded in the questionnaires compiled by the patients. The values were compared by statistical analysis (Student's t-distribution) to check for significant variations between the initial values and those recorded over the course of treatment. The results demonstrate an improvement in the quality of life in all eight domains. Considerable benefits were already observed after the first three months, and patients who continued treatment for longer periods showed additional improvements in subsequent follow-ups. The domain regarding limitations to personal role due to problems of physical health exhibits a change from an initial 0, to 50 after three months, and 100 in subsequent assessments. This means that these patients resumed all their normal activities, including work. In the domain regarding limitations to personal role due to emotional problems, there is a change from an initial 0, to 66 after three months, and a stable 100 in subsequent assessments. This indicates achievement of emotional wellbeing over the course of treatment. The questionnaires were processed on the website of the Mario Negri Institute, where values are calculated for each domain and then compared to a standard sample by age and gender.

SF 36 area		start n=100	1 st FU n=49	start/1 st FU	2 nd FU n=32	start/2 nd FU	3 rd FU n=18	start/3 rd FU	4 th FU n=8	start/4 th FU
		median/area			med/a		med/a		med/a	
Physical activity	AF	65	85	p < 0.0001	95	p < 0.0001	95	p < 0.0001	95	p = 0.0022

Limitations to personal role due to problems of physical health	LAF	0	50	p < 0.0001	100	p < 0.0001	100	p < 0.0001	100	p < 0.0001
Physical pain	DF	41	61	p < 0.0001	74	p < 0.0001	73	p < 0.0001	67	p = 0.0025
General health	SG	33	52	p < 0.0001	56	p < 0.0001	50	p = 0.0001	51	p = 0.0016
Vitality	V	35	55	p < 0.0001	60	p < 0.0001	65	p < 0.0001	65	p = 0.0002
Social activity	AS	37	75	p < 0.0001	87	p < 0.0001	87	p < 0.0001	94	p < 0.0001
Limitations to personal role due to emotional problems	LAE	0	66	p < 0.0001	100	p < 0.0001	100	p < 0.0001	100	p < 0.0001
Mental Health	SM	55	72	p < 0.0001	80	p < 0.0001	80	p < 0.0001	84	p < 0.0001
Areas with reductions > 10% relative to standard group by age and gender of the general population		5	1	p < 0.0001	0	p < 0.0001	0	p < 0.0001	0	p < 0.0001
start = recruitment of patients; FU = follow-up										
Statistical tests: Student's t-distribution										

Table 2. Results obtained using the SF36 questionnaire on the 100 patients included in the study: the median values for the individual domains in the first questionnaire (start) are compared with those from the subsequent questionnaires (at 3 months, 6 months, 9 months, and 12 months).

Figure 2 shows in detail the variations in median values for the individual domains in the initial questionnaire and over the course of the follow-ups.

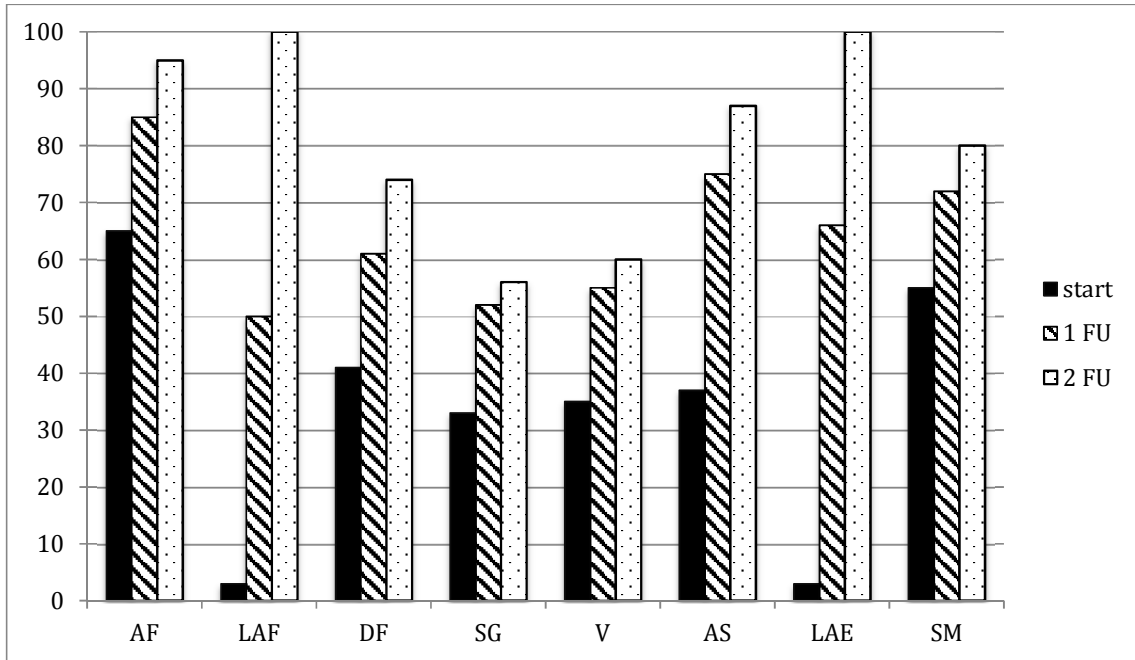


Figure 2. Initial median values and over the course of the follow-ups for each individual domain in the SF36 questionnaire.

What appears most impressive is that the differences in values between patients and the general population for the various domains of the questionnaire disappeared over the course of treatment (Figure 3).

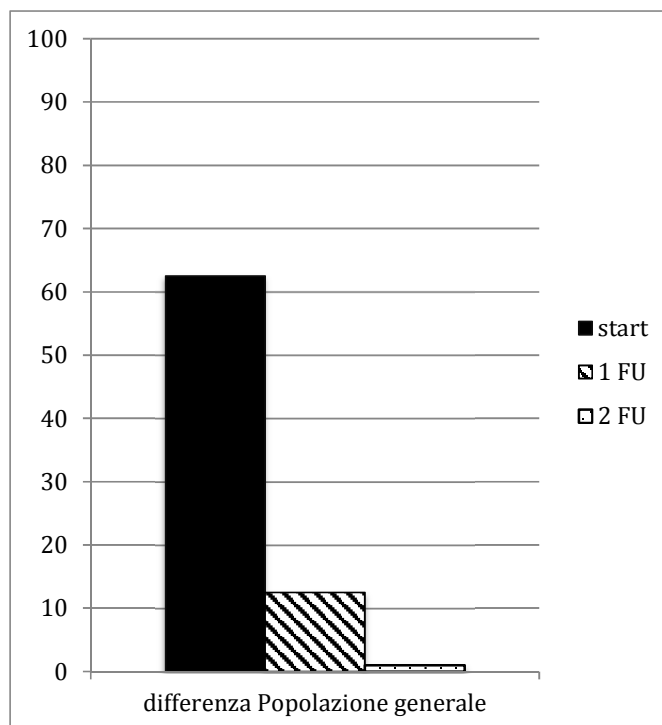


Figure 3. Percentage differences between the values from the SF36 questionnaire compared to the standard general population group by age and gender. The initial percentage was above 60%, falling to 0% by the third follow-up.

Figure 4 shows the number of patients included in the study over the four quarters, with a clear increase in patients participating in the fourth quarter, probably due to the good results achieved by patients taking part in the previous quarters.

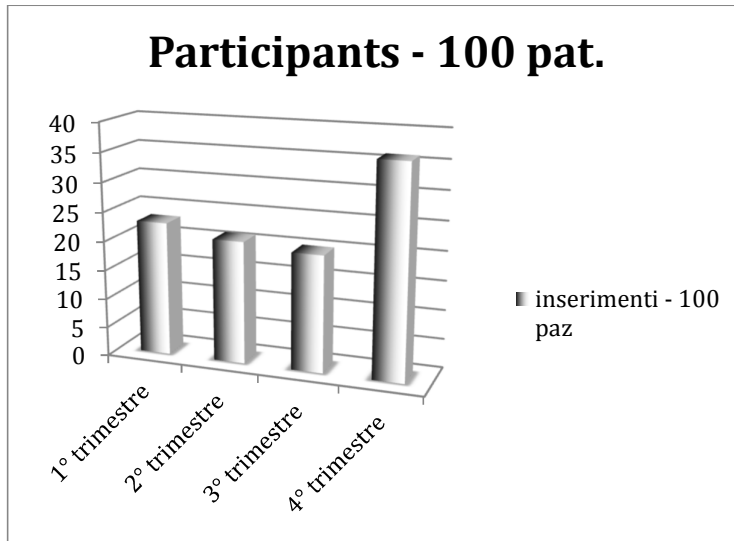


Figure 4. Number of patients taking part in the study over the four quarters.

For patients undergoing chemotherapy, integrated medicine was offered for the entire duration of the chemotherapy cycles, with the aim of reducing the side effects of the treatment and so improving quality of life. Regardless of the type of tumor and stage of the same, the majority of patients experienced an improvement in quality of life, which according to American and European studies has a positive influence on survival.

Discussion

The results achieved are highly significant, because studies on large numbers of oncology cases have demonstrated that the quality of life of patients correlates positively with survival even for advanced stage tumors. In one study conducted on 391 patients affected by non-small cell pulmonary tumor in advanced stage it was observed that a change in quality of life correlated with health over the course of treatment was a significant prognostic factor for survival, (23). In another study involving 3700 patients conducted at the Mayo Clinic, the quality of life scores matched a net variation in average survival of patients from 12.3 months for patients with low scores to 18.4 months for patients with high scores (7). In a meta-analysis of 30 trials by EORTC involving 10,000 patients, Quinteen and colleagues revealed that the physical and emotional functions of patients including asthenia, nausea, vomiting, and loss of appetite significantly influenced survival (8). The integrated medicine offered to patients at the Gallino Hospital is oriented towards improving quality of life and reducing the side effects of chemotherapy and thus, on the basis of the data presented, in itself promotes the survival of patients. Integrated medicine

reduces the side effects of chemotherapy and therefore offers savings in health costs. These include: reduced use of pharmaceuticals to limit myelosuppression, nausea, and vomiting; reduced expenses from infective complications and hospitalization; reduced expenses for analgesic and antidepressant pharmaceuticals. Many patients were also able to resume work, thereby reducing social costs. It was observed that a change in quality of life correlated with health over the course of treatment was a significant prognostic factor for survival, (23) and the improvement of survival is a saving on health cost. We have reported a rapid improvement of limitations to personal role due to problems of physical and emotional health. This means that these patients resumed all their normal activities, including work and that achieved emotional wellbeing over the course of treatment. This is very important because the patient in a short time recovers his/her role in society and gradually does not need the support of "care givers". Caregivers are usually relatives who need to stop their work to care for patients. This involves social spending, in addition with an improvement in the delicate relationship between patients and caregivers (24)

It is worth remembering the problems encountered by patients who have been successfully treated for neoplasia and classed as "long-term survivors". Studies conducted on long-term survivors of Hodgkin's and non-Hodgkin's lymphoma revealed that they have to face specific problems deriving from chronic medical and psycho-social complications, which can heavily compromise their quality of life correlated with health. Asthenia, depression, breakdown of family relations, and fertility problems are the main issues for these patients (25-27), in addition to late complications like induced tumors and cardiovascular diseases, the incidence of which is considerably higher than in the general population (28). Mols F et al sustain that integrated medicine can offer long-term survivors an improvement in quality of life in physical and psychological terms sufficient to enable full re-integration into society, and a preventive action against the late risks associated with previous treatments (29).

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Name	Gender	Age	Pathology	Onset	Associated path.	Origin	Start IM
AO	F	48	LNH	July-10	Vasculitis 2007	Gallino Hematology	Feb-17
BG	F	58	K-ras lung	April-17		Micone Hospital	April-17
BS	F	48	K-ras breast	May-17		Micone Hospital	Oct-17
BE	F	50	K-ras breast	Oct-14		Galliera Hospital	Oct-17
BM	F	55	K-ras breast	Oct-13		IRCS S Martino	Nov-17
BE	F	63	K-ras breast	Jan-02		Villa Scassi Hospital	Nov-17
BS	M	55	K-ras pancreas	mar-16		Micone Hospital	Oct-17
CA	M	78	LNH	Dec-16		Gallino Hematology	Feb-17
CO	F	52	K-ras breast	Oct-16		Galliera Hospital	July-17
CS	F	50	Chronic lymph. leuk.	mar-12		Gallino Hematology	May-17
CP	F	67	K-ras breast	mar-10		Gallino Oncology	June-17
CT	F	43	Acute lymph. leuk.	June-94		Gallino Hematology	mar-17
CA	F	47	K-ras breast	June-01	LH 1987	Gallino Hematology	April-17
CC	F	54	K-ras breast	Oct-16		Villa Scassi Hospital	Oct-17
CV	F	65	Mesothelioma	mar-16		Villa Scassi Hospital	July-17
CA	F	45	K-ras breast	June-16		IRCS S Martino	May-17
CMR	F	54	K-ras pancreas	Oct-15	K-ras breast 1998	Gallino Hematology	mar-17
CMC	F	52	K-ras breast	July-15		Micone Hospital	Feb-17
CR	F	47	K-ras breast	June-06	LH 1985	Gallino Hematology	April-17
CN	F	63	Glioblastoma	Jan-16		Humanitas (MI)	Aug-17
CP	F	60	K-ras breast	April-04		IRCS S Martino	Nov-17
DMA	F	60	K-ras pancreas	July-16		Galliera Hospital	Nov-17
DA	M	77	LNH	Nov-16		IRCS S Martino	Feb-17
DG	M	51	K-ras rectum	mar-17		IRCS S Martino	June-17
DG	M	71	K-ras colon	July-17		IRCS S Martino	Nov-17
DMA	F	75	Carcinosarcoma	May-17	K-ras rectum 2013	Galliera Hospital	June-17
DF	F	61	K-ras breast	Aug-17		Micone Hospital	Sep-17
DG	F	80	K-ras breast	mar-16		Galliera Hospital	July-17
DG	F	60	K-ras breast	mar-16	LNH 2003	Gallino Hematology	Feb-17
FM	F	51	K-ras breast	May-16		Micone Hospital	April-17
FL	F	45	K-ras breast	Aug-17		Villa Scassi Hospital	Oct-17
FM	M	31	Astrocytoma	June-14		Galliera Hospital	Oct-17
FL	F	53	LH	March-92		Gallino Hematology	Feb-17
GG	M	18	LH	Jan-15		Gallino Hematology	mar-17
GA	F	67	K-ras breast	Jan-13		IRCS S Martino	Nov-17
GG	M	62	LNH	Dec-13		IRCS S Martino	Dec-17
GD	F	43	HD	May-15	APS 2011	Gallino Hematology	April-17
GR	F	71	K-ras breast	July-85		Gallino Oncology	April-17
IO	F	71	K-ras breast	June-97		Galliera Hospital	mar-17
IP	F	44	K-ras breast	Dec-13		IEO (MI)	Oct-17
LR	M	52	K-ras lung	June-17		IRCS S Martino	mar-17
LM	F	60	LH	June-82		Gallino Hematology	June-17
LA	F	77	LNH	June-03	Sjogren 1995	Gallino Hematology	Feb-17
LG	M	53	K-ras kidney	Nov-13		Gallino Oncology	Sep-17
LR	F	78	K-ras breast	July-98		Galliera Hospital	June-17

LE	F	43	K-ras breast	Jan-14		Micone Hospital	Oct-17
LC	F	59	K-ras breast	Feb-13		Galliera Hospital	Oct-17
LM	F	67	K-ras uterus	May-14		Galliera Hospital	July-17
LF	F	51	K-ras breast	Jan-13		Gallino Oncology	Nov-17
MC	M	74	LNH	Feb-16		Gallino Hematology	Feb-17
MP	F	45	LH	Jan-02		IRCS S Martino	Nov-17
NV	M	47	Mesothelioma	Feb-14		Gallino Oncology	June-17
NC	F	53	K-ras ovary	April-16		Galliera Hospital	Sep-17
PV	F	33	LH	July-09		Gallino Hematology	mar-17
PML	F	81	Waldestrom	Feb-14		Gallino Hematology	Aug-17
PF	M	58	K-ras lung	June-17		IRCS S Martino	Dec-17
PM	M	58	LNH	Nov-16		Gallino Hematology	mar-17
PV	F	39	K-ras breast	Feb-17		Micone Hospital	June-17
PS	M	53	LH	Feb-16		Gallino Hematology	Jan-17
PI	F	38	K-ras breast	Nov-14		Galliera Hospital	May-17
PM	F	58	K-ras breast	Jan-15		Sampierdarena	Nov-17
PD	F	38	K-ras ovary	May-12		IEO (MI)	Oct-17
PT	F	79	K-ras ovary	June-17	Connective tissue 2000	Gallino Hematology	mar-17
PR	F	61	K-ras breast	Jan-16	K-ras utero 2004	IRCS S Martino	May-17
PML	F	53	K-ras ovary	Aug-17		IRCS S Martino	Nov-17
QMA	F	59	K-ras ovary	May-17	Churg Strauss 2006	Gallino Hematology	July-17
RP	M	50	Melanoma	Jan-14		IRCS S Martino	May-17
RR	F	66	K-ras lung	Feb-14		IRCS S Martino	July-17
RC	F	55	K-ras larynx	Feb-16	Dermatomyositis 2013	Gallino Hematology	Feb-17
			K-ras sigmoid colon				
SAE	F	56		June-15		Galliera Hospital	July-17
SR	M	56	K-ras colon	Feb-17		Galliera Hospital	Oct-17
SC	F	83	K-ras breast	Aug-16		Micone Hospital	Oct-17
SA	F	53	K-ras breast	Jan-08		Galliera Hospital	Sep-17
TCM	F	81	K-ras breast	Jan-93		Galliera Hospital	Feb-17
TF	F	50	K-ras breast	July-16		Micone Hospital	Oct-17
VV	F	49	K-ras ovary	Nov-16		Galliera Hospital	Sep-17
VFG	M	62	K-ras rectum	Dec-15		Galliera Hospital	mar-17
VL	F	63	K-ras pancreas	Jan-17		Galliera Hospital	Aug-17
ZP	M	52	K-ras colon	Nov-16		Galliera Hospital	July-17

Attachment 1. Characteristics of patients. Details include: age, gender, oncological diagnosis, onset of oncological pathology, associated pathology with year of onset, referring oncology department, and starting date of integrated medical treatment.

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