

FARMACI CON USO CONSOLIDATO NEL TRATTAMENTO DEI TUMORI SOLIDI NELL'ADULTO PER INDICAZIONI ANCHE DIFFERENTI DA QUELLE PREVISTE DAL PROVVEDIMENTO DI AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO

<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
Anastrozolo	Trattamento del tumore della mammella maschile in fase avanzata, in associazione a LHRH analogo, in casi di fallimento di tamoxifen o intolleranza a tale farmaco	<p><u>White J. et al</u>, Male breast carcinoma: increased awareness needed. Breast Cancer Research, 2011</p> <p><u>Cardoso F. et al</u>, 1st international consensus guideline for advanced breast cancer (ABC 1). Breast 2012</p> <p><u>Korde L.A. et al</u>, Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol 2010</p> <p><u>Giordano S.H., Hortobagay GN.</u> Leuprolide acetate plus aromatase inhibition for male breast cancer. J Clin Oncol 2006</p> <p><u>Linee guida AIOM</u>-Neoplasie della mammella, edizione 2018</p>

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	<p>Utilizzo in monoterapia nel carcinoma ovarico recidivato</p>	<p><u>NCCN guidelines- Ovarian Cancer, version 2.2018</u> <u>Rao G.G., Miller DS.</u> Hormonal therapy in epithelial ovarian cancer. Expert Rev Anticancer Ther 2006 <u>Papadimitriou C.A. et al,</u> Hormonal therapy with letrozole for relapsed epithelial ovarian cancer. Long-term results of a phase II study. Oncology 2004 <u>Bowman A. et al,</u> CA125 response is associated with estrogen receptor expression in a phase II trial of letrozole in ovarian cancer: identification of an endocrine-sensitive subgroup. Clin Cancer Res 2002 <u>del Carmen M.G. et al,</u> Phase II trial of anastrozole in women with asymptomatic mullerian cancer. Gynecol Oncol 2003 <u>Ramirez P.T. et al,</u> Efficacy of letrozole in the treatment of recurrent platinum- and taxane-resistant high-grade cancer of the ovary or peritoneum. Gynecol Oncol 2008 <u>Serkies K. et al,</u> The role of hormonal factors and endocrine therapy in ovarian cancer. Współczesna Onkologia/Contemporary Oncology 2013</p>
	<p>Trattamento di pazienti in premenopausa con carcinoma mammario metastatico e recettori ormonali positivi in associazione a LHRH analogo (con accertata controindicazione a tamoxifen):</p>	<p><u>Carlson R.W. et al,</u> Phase II trial of anastrozole plus goserelin in the treatment of hormone receptor-positive, metastatic carcinoma of the breast in premenopausal women. J Clin Oncol. 2010 <u>Linee guida AIOM-Neoplasie della mammella, edizione 2017</u></p>
<p>Bleomicina</p>	<p>Utilizzo, da solo o in associazione, nei tumori solidi.</p>	<p><u>DeVita V.T. et al,</u> Cancer: Principles and Practice of Oncology, 6th Ed. <u>Bonadonna. G. et al,</u> Medicina Oncologica, Settima Edizione.</p>

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Calcio Levofolinato	Utilizzo senza restrizione in associazione alle fluoropirimidine	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed. <u>Bonadonna. G. et al</u> , Medicina Oncologica, Settima Edizione.
Capecitabina	Come alternativa al fluorouracile dove non si ritenga opportuno o indicato un trattamento infusioneale	<u>Cassidy J, et al</u> . First-line oral capecitabine therapy in metastatic colorectal cancer: a favorable safety profile compared with intravenous 5-fluorouracil/leucovorin. Ann Oncol. 2002; 566-75. <u>Van Cutsem E, et al</u> . Oral capecitabine vs intravenous 5-fluorouracil and leucovorin: integrated efficacy data and novel analyses from two large, randomised, phase III trials. Br J Cancer. 2004; 90(6):1190-7.
	In associazione a vinorelbina in pazienti con tumore della mammella localmente avanzato o metastatico pre-trattate con antraciclina e/o taxani	Linee guida AIOM-Neoplasie della mammella, edizione 2018
Carboplatino	Utilizzo, da solo o in associazione, nei tumori solidi e in particolare: alternativa al cisplatino quando questo è controindicato	<u>Kim E. et al</u> , Comparison of cisplatin/etoposide versus carboplatin/etoposide concurrent chemoradiation therapy for limited-stage small cell lung cancer (LS-SCLC) in the elderly population (age >65 years) using national SEER-Medicare data. Pract Radiat Oncol. 2016 <u>Tanvetyanon T. et al</u> , Use of Adjuvant Cisplatin-Based Versus Carboplatin-Based Chemotherapy in Non-Small-Cell Lung Cancer: Findings From the Florida Initiative for Quality Cancer Care. J Oncol Pract. 2015

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	Utilizzo nel seminoma	<u>Oliver R.T. et al</u> , Randomized trial of carboplatin versus radiotherapy for stage I seminoma: mature results on relapse and contralateral testis cancer rates in MRC TE19/EORTC 30982 study (ISRCTN27163214). J Clin Oncol. 2011
	Trattamento del mesotelioma pleurico in caso di controindicazione o intolleranza a cisplatino	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed. <u>Bonadonna. G. et al</u> , Medicina Oncologica, Settima Edizione. Linee Guida NCI 2006. <u>Srouf S.A. et al.</u> , <i>Pemetrexed in combination with cisplatin versus carboplatin as first-line therapy in patients with advanced-stage malignant pleural mesothelioma (MPM): A systematic review and meta-analysis. ASCO 2016</i>
	In combinazione con paclitaxel nel trattamento del melanoma metastatico	<u>Flaherty K.T. et al</u> , Phase III trial of carboplatin and paclitaxel with or without sorafenib in metastatic melanoma. J Clin Oncol 2013 <u>Kottschade L.A. et al</u> , A phase II trial of nab-paclitaxel (ABI-007) and carboplatin in patients with unresectable stage IV melanoma: a North Central Cancer Treatment Group Study, N057E(1). Cancer 2011 <u>Pflugfelder A. et al</u> , Effectiveness of carboplatin and paclitaxel as first- and second-line treatment in 61 patients with metastatic melanoma. PLoS One 2011
	In associazione al taxolo, nel trattamento del melanoma metastatico	<u>Flaherty KT et al</u> . Phase III trial of carboplatin and paclitaxel with or without sorafenib in metastatic melanoma. J Clin Oncol 2013; 31:373-379. <u>Kottschade LA et al</u> . A randomized phase 2 study of temozolomide and bevacizumab or nab-paclitaxel, carboplatin, and bevacizumab in patients with unresectable stage IV melanoma: a North Central Cancer Treatment Group study, N0775. Cancer 2013; 119:586-592. <u>Kottschade LA et al</u> . A phase II trial of nab-paclitaxel (ABI-007) and carboplatin in patients with unresectable stage IV melanoma: a North Central Cancer

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		Treatment Group Study, N057E(1). Cancer 2011; 117:1704-1710. Pflugfelder A et al. Effectiveness of carboplatin and paclitaxel as first- and second-line treatment in 61 patients with metastatic melanoma. PLoS One 2011;6:e16882.
Ciclofosfamide	Utilizzo ad alte dosi nei regimi di condizionamento pre-trapianto	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed. <u>Mielcarek M. et al</u> , Posttransplantation cyclophosphamide for prevention of graft-versus-host disease after HLA-matched mobilized blood cell transplantation. Blood. 2016
Cisplatino	<p>In monoterapia o in associazione, nei tumori solidi e in particolare:</p> <ul style="list-style-type: none"> • Carcinoma della mammella • Mesotelioma pleurico • Carcinoma dello stomaco • Carcinoma spinocellulare della cute • Carcinoma del pancreas • Neoplasie cerebrali • Carcinoma della cervice uterina • Neoplasie a sede primitiva ignota • Colangiocarcinoma • Carcinoma delle vie biliari 	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed. <u>Bonadonna. G. et al</u> , Medicina Oncologica, Settima Edizione.

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Docetaxel	<p>Trattamento del carcinoma gastrico e della giunzione gastroesofagea, anche in monoterapia</p>	<p><u>Ajani J.A.</u> Optimizing docetaxel chemotherapy in patients with cancer of the gastric and gastroesophageal junction evolution of the docetaxel, cisplatin, and 5-fluorouracil regimen. Cancer 2008</p>
	<p>Trattamento del carcinoma ovarico recidivato dopo paclitaxel, in monoterapia o in associazione con altri chemioterapici</p>	<p><u>Ferrandina G. et al</u>, Docetaxel and oxaliplatin in the second-line treatment of platinum-sensitive recurrent ovarian cancer: a phase II study. Ann Oncol. 2007</p> <p><u>Kushner D.M. et al</u>, Weekly docetaxel and carboplatin for recurrent ovarian and peritoneal cancer: a phase II trial. Gynecol Oncol. 2007</p> <p><u>Tinker A.V. et al</u>, Phase II trial of weekly docetaxel for patients with relapsed ovarian cancer who have previously received paclitaxel--ANZGOG 02-01. Gynecol Oncol. 2007</p> <p><u>Strauss H.G. et al</u>, Phase II trial of docetaxel and carboplatin in recurrent platinum-sensitive ovarian, peritoneal and tubal cancer. Gynecol Oncol. 2007</p> <p><u>Polyzos A. et al</u>, Docetaxel in combination with irinotecan (CPT-11) in platinum-resistant paclitaxel-pretreated ovarian cancer. Anticancer Res. 2005</p> <p><u>Piccart M.J. et al</u>, Docetaxel: an Active New Drug for Treatment of Advanced Epithelial Ovarian Cancer JNCI J Natl Cancer Inst 1995</p>

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	<p>Trattamento di prima linea del carcinoma ovarico in combinazione con derivati del platino, in caso di reazioni di ipersensibilità al paclitaxel.</p>	<p><u>Vasey P.A. et al</u>, Phase III randomized trial of docetaxel-carboplatin vs paclitaxel-carboplatin as first line chemotherapy for ovarian carcinoma J Natl cancer Inst 2004</p>
	<p>In combinazione con ciclofosfamide, nel trattamento adiuvante del carcinoma mammario, in pazienti non candidabili a terapia con antracicline</p>	<p><u>Jones S.E. et al</u>, Phase III trial comparing doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. J Clin Oncol 2006</p>
	<p>Trattamento adiuvante del tumore della mammella, in regime sequenziale dopo chemioterapia con antracicline, in pazienti con linfonodi positivi</p>	<p><u>Rochè H. et al</u>, Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: the FNCLCC PACS 01 Trial. J Clin Oncol. 2006</p>

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	<p>Trattamento adiuvante del tumore della mammella, in pazienti con linfonodi negativi ad alto rischio, nell'ambito di schemi di polichemioterapia o terapia impiegati nelle pazienti con linfonodi positivi.</p>	<p><u>De Laurentiis M. et al</u>, Taxane-based combinations as adjuvant chemotherapy of early breast cancer: a meta-analysis of randomized trials. J Clin Oncol. 2008</p> <p><u>Estévez L.G. et al</u>, Evidence-based use of taxanes in the adjuvant setting of breast cancer. A review of randomized phase III trials. Cancer Treat Rev. 2007</p> <p><u>Linee guida AIOM-Neoplasie della mammella</u>, edizione 2018</p>
	<p>Trattamento neoadiuvante del tumore della mammella operabile ad alto rischio, in combinazione con antracicline (utilizzo concomitante o sequenziale), o altri chemioterapici attivi in tale neoplasia.</p>	<p><u>NCCN Clinical Practice Guidelines in Oncology-Breast Cancer</u>, version 1.2018</p>
	<p>Trattamento dei sarcomi delle parti molli in combinazione con gemcitabina</p>	<p><u>Maki R.G.</u> Gemcitabine and docetaxel in metastatic sarcoma: past, present and future. Oncologist, 2007</p> <p><u>NCCN Clinical Practice Guidelines in Oncology- Soft Tissue Sarcoma</u>, version 2.2018</p>

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	<p>Trattamento dei pazienti adulti con carcinoma della prostata ormonosensibile metastatico.</p>	<p><u>Sweeney C et al.</u> Impact on overall survival (OS) with chemohormonal therapy versus hormonal therapy for hormone-sensitive newly metastatic prostate cancer (mPrCa): An ECOG-led phase III randomized trial. J Clin Oncol 2014; 32:5s (suppl; abstr LBA2).</p> <p><u>Sweeney C. et al.</u>, Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer. N Engl J Med 2015.</p> <p><u>James N.D. et al.</u>, Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. Lancet. 2016</p> <p><u>Vale C.L. et al.</u>, Addition of docetaxel or bisphosphonates to standard of care in men with localised or metastatic, hormone-sensitive prostate cancer: a systematic review and meta-analyses of aggregate data. Lancet Oncol. 2016</p>
	<p>Trattamento del carcinoma squamoso dell'esofago avanzato.</p>	<p><u>Muro K, et al.</u> A single-phase II study of single agent docetaxel in patients with metastatic esophageal cancer. Ann Oncol. 2004; 15: 955-9.</p>
<p>Doxorubicina</p>	<p>In monoterapia o in associazione, nei tumori solidi ed in particolare in tutti i tipi di sarcomi in cui si ritiene indicato.</p>	<p><u>DeVita V.T. et al.</u>, Cancer: Principles and Practice of Oncology, 6th Ed</p> <p><u>Bonadonna G. et al.</u>, Medicina Oncologica, Settima Edizione</p>

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Doxorubicina liposomiale Pegilata (Caelyx)	Trattamento del sarcoma di Kaposi non correlato a infezione da HIV.	<u>Volkow P. et al</u> , Triple secondary neoplasms: penis, lip and oral cavity in an AIDS patient treated with pegylated liposomal doxorubicin for cutaneous Kaposi's sarcoma. AIDS 2014
	Trattamento dei sarcomi dei tessuti molli recidivati o metastatici in pazienti con controindicazioni all'impiego di antracicline convenzionali per rischio cardiologico.	<u>Judson I. et al</u> , Randomised phase II trial of pegylated liposomal doxorubicin (DOXIL/CAELYX) versus doxorubicin in the treatment of advanced or metastatic soft tissue sarcoma: a study by the EORTC Soft Tissue and Bone Sarcoma Group. Eur J Cancer 2001
	In associazione con cisplatino/carboplatino nelle neoplasie ovariche	<u>Pujade-Lauraine E. et al</u> , Pegylated liposomal Doxorubicin and Carboplatin compared with Paclitaxel and Carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010 <u>NICE technology appraisal guidance</u> : Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer (27 April 2016)
	In associazione con carboplatino nel trattamento di prima linea del carcinoma ovarico in pazienti allergiche o intolleranti a paclitaxel	<u>Pignata S. et al</u> , Carboplatin plus paclitaxel versus carboplatin plus pegylated liposomal doxorubicin as first-line treatment for patients with ovarian cancer: the MITO-2 randomized phase III trial. J Clin Oncol 2011
Eparine a basso peso molecolare (originatore o biosimilare)	Profilassi delle trombosi venose profonde in pazienti oncologici ambulatoriali a rischio (KHORANA ≥ 3)[con condizione che l'indicazione sia posta dallo specialista ematologo o oncologo]	<u>Mandalà M. et al</u> , Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines. Ann Oncol, 2011 <u>Lyman G.H. et al</u> , Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol, 2013 <u>Linee guida AIOM-Tromboembolismo venoso in pazienti con tumori solidi</u> , edizione 2017

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	<p>Profilassi delle trombosi venose profonde in pazienti a rischio affetti da mieloma multiplo, sulla base del giudizio clinico individuale</p>	<p><u>Mandalà M. et al</u>, Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines. Ann Oncol, 2011</p> <p><u>Lyman G.H. et al</u>, Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol, 2013</p> <p><u>Linee guida AIOM-Tromboembolismo venoso in pazienti con tumori solidi</u>, edizione 2017</p>
<p>Epirubicina</p>	<p>In monoterapia o in associazione, nel trattamento dei tumori solidi, sia in fase precoce sia avanzata, in sostituzione della doxorubicina</p>	<p><u>DeVita V.T. et al</u>, Cancer: Principles and Practice of Oncology, 6th Ed</p> <p><u>Bonadonna. G. et al</u>, Medicina Oncologica, Settima Edizione</p>
<p>Exemestane</p>	<p>Trattamento del tumore della mammella maschile in fase avanzata, in associazione a LHRH analogo, in casi di fallimento di tamoxifen o intolleranza a tale farmaco. (Si intende autorizzato lo schema terapeutico dell'associazione)</p> <p>In associazione a LHRH analogo nel trattamento del carcinoma mammario metastatico in premenopausa</p>	<p><u>White J. et al</u>, Male breast carcinoma: increased awareness needed. Breast Cancer Research, 2011</p> <p><u>Cardoso F. et al</u>, 1st international consensus guideline for advanced breast cancer (ABC 1). Breast 2012</p> <p><u>Korde L.A. et al</u>, Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol 2010</p> <p><u>Giordano S.H., Hortobagay GN.</u> Leuprolide acetate plus aromatase inhibition for male breast cancer. J Clin Oncol 2006</p> <p><u>Linee guida AIOM-Neoplasie della mammella</u>, edizione 2017</p> <p><u>Pagani O. et al</u>, Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. N Engl J Med 2014</p>

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Fluorouracile	In monoterapia o in associazione, nel trattamento dei tumori solidi	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed <u>Bonadonna G. et al</u> , Medicina Oncologica, Settima Edizione
Fulvestrant	Trattamento del tumore della mammella maschile in fase avanzata, in associazione a LHRH analogo, in casi di fallimento di tamoxifen o intolleranza a tale farmaco. (Si intende autorizzato lo schema terapeutico dell'associazione)	<u>Masci G. et al</u> , Fulvestrant for advanced male breast cancer patients: a case series Ann Oncol 2011 <u>Zagouri F. et al</u> , Fulvestrant and male breast cancer: a case series. Ann Oncol 2013 <u>de la Haba Rodríguez J.R. et al</u> , Fulvestrant in advanced male breast cancer. Ann Oncol 2009 <u>Agrawal A. et al</u> , Fulvestrant in advanced male breast cancer. Breast Cancer Res Treat 2007 <u>Tan W.W. et al</u> , N0539 phase II trial of fulvestrant and bevacizumab in patients with metastatic breast cancer previously treated with an aromatase inhibitor: a North Central Cancer Treatment Group (now Alliance) trial. Ann Oncol 2013
Gemcitabina	Terapia di salvataggio della neoplasia germinale del testicolo	<u>Linee guida AIOM-Tumore del testicolo</u> , edizione 2018.

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	Trattamento dei sarcomi dei tessuti molli	<u>Casali P.G. et al</u> , Soft tissue sarcomas: ESMO Clinical Recommendations for diagnosis, treatment and follow-up. Annals of Oncology 2009
	Trattamento del colangiocarcinoma e del carcinoma delle vie biliari	<u>Linee guida AIOM</u> - Tumori delle vie biliari, edizione 2018. <u>Valle J. et al</u> , Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med 2010. <u>Squadroni M. et al</u> , Cholangiocarcinoma. Critical Reviews in Oncology/hematology 2017.
	Trattamento delle neoplasie del distretto cervico-facciale	<u>Linee guida AIOM</u> - Tumori della Testa e del Collo, edizione 2018.
	In monoterapia o in associazione con antracicline o derivati del platino nel trattamento del carcinoma ovarico recidivato	<u>Tas F. et al</u> , A pilot study evaluating the efficacy and toxicity of biweekly gemcitabine and pegylated liposomal doxorubicin in recurrent platinum-resistant epithelial ovarian cancer. Int J Clin Oncol. 2008 <u>Kalykaki A. et al</u> , Gemcitabine plus oxaliplatin (GEMOX) in pretreated patients with advanced ovarian cancer: a multicenter phase II study of the Hellenic Oncology Research Group (HORG). Anticancer Res. 2008 <u>Ferrandina G. et al</u> , Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian

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		<p>cancer. J Clin Oncol. 2008</p> <p><u>Germano D. et al</u>, Gemcitabine combined with oxaliplatin (GEMOX) as salvage treatment in elderly patients with advanced ovarian cancer refractory or resistant to platinum: a single institution experience. J Chemother. 2007</p> <p><u>Pectasides D. et al</u>, Gemcitabine and pegylated liposomal doxorubicin alternating with cisplatin plus cyclophosphamide in platinum refractory/resistant, paclitaxel-pretreated, ovarian carcinoma. Gynecol Oncol. 2008</p> <p><u>Mutch D.G. et al</u>, Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer. J Clin Oncol. 2007</p> <p><u>Harnett P. et al</u>, Phase II study of gemcitabine and oxaliplatin in patients with recurrent ovarian cancer: an Australian and New Zealand Gynaecological Oncology Group study. Int J Gynecol Cancer. 2007</p> <p><u>Bozas G. et al</u>, Biweekly gemcitabine and cisplatin in platinum resistant/refractory, paclitaxel-pretreated, ovarian and peritoneal carcinoma. Gynecol Oncol. 2007</p> <p><u>Pfisterer J. et al</u>, Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGOVAR, the NCIC CTG, and the EORTC GCG. J Clin Oncol. 2006</p> <p><u>Galligioni E. et al</u>, Gemcitabine and anthracyclines in platinum-resistant ovarian cancer. Ann Oncol. 2006</p> <p><u>Safra T. et al</u>. Heavily pretreated ovarian cancer patients treated by single-agent gemcitabine. A retrospective outcome comparison between platinum-sensitive and platinum-resistant patients. Acta Oncol. 2006.</p>

<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
	<p>In monoterapia o in associazione nel trattamento del carcinoma mammario metastatico in pazienti pretrattate</p>	<p><u>Triphaty D.</u> Overview: gemcitabine as single-agent therapy for advanced breast cancer. Clin Breast Cancer 2002 <u>Park J.S. et al,</u> Phase II gemcitabine and capecitabine combination therapy in recurrent or metastatic breast cancer patients pretreated with anthracycline and taxane. Cancer Chemother Ther 2014 <u>Laessig D. et al,</u> Gemcitabine and carboplatin in intensively pretreated patients with metastatic breast cancer. Oncology 2007</p>
	<p>Trattamento adiuvante del carcinoma del pancreas</p>	<p><u>Bonadonna G. et al,</u> Medicina Oncologica 8° edizione <u>Oettle H. et al,</u> Adjuvant chemotherapy with gemcitabine vs observation in patients undergoing curative intent resection of pancreatic cancer: a randomized controlled trial. JAMA 2007</p>
	<p>In monoterapia o in associazione a platino, nel trattamento del carcinoma dell'endometrio e della cervice uterina</p>	<p><u>Brown J. et al,</u> Combination of gemcitabine and cisplatin is highly active in women with endometrial carcinoma: results of a prospective phase 2 trial. Cancer 2010 <u>Monk B.J. et al,</u> Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: a Gynecologic Oncology Group study. J Clin Oncol. 2009</p>

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	<p>In monoterapia o in associazione con cisplatino o carboplatino, nel trattamento del mesotelioma</p>	<p><u>Kalmadi S.R. et al</u>, Gemcitabine and cisplatin in unresectable malignant mesothelioma of the pleura: a phase II study of the Southwest Oncology group (SWOG 9810). Lung Cancer 2008</p> <p><u>Nowak A.K. et al</u>, A multicentre phase II study of cisplatin and gemcitabine for malignant mesothelioma. Br J Cancer 2002</p> <p><u>Favaretto A.G. et al</u>, Gemcitabine combined with carboplatin in patients with malignant pleural mesothelioma: a multicentric phase II study. Cancer 2003</p>
	<p>Trattamento dei tumori epiteliali del timo pretrattati</p>	<p><u>Palmieri et al.</u> Capecitabine plus gemcitabine in thymic epithelial tumors: final analysis of the phase II trial. Future Oncol. 2014; 10 (14): 2141-47.</p>
<p>Idrossiurea (idrossicarbamide)</p>	<p>Trattamento dei tumori cerebrali e meningiomi:</p>	<p><u>Schrell U.M. et al</u>, Hydroxyurea for treatment of unresectable and recurrent meningiomas. I. Inhibition of primary human meningioma cells in culture and in meningioma transplants by induction of the apoptotic pathway. J Neurosurg. 1997</p> <p><u>Schrell U.M. et al</u>, Hydroxyurea for treatment of unresectable and recurrent meningiomas. II. Decrease in the size of meningiomas in patients treated with hydroxyurea. J Neurosurg. 1997</p> <p><u>Newton H.B. et al</u>, Hydroxyurea chemotherapy for unresectable or residual meningioma. J Neurooncol. 2000</p> <p><u>Mason, W.P. et al</u>, Stabilization of disease progression by hydroxyurea in patients with recurrent or unresectable meningioma. J Neurosurg. 2002</p> <p><u>Rosenthal M.A. et al</u>, Treatment of high risk or recurrent meningiomas with hydroxyurea. J Clin Neurosci. 2002</p> <p><u>Loven D. et al</u>, Non-resectable slow-growing meningiomas treated by hydroxyurea. J Neurooncol. 2004</p>

<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
Ifosfamide	In monoterapia o in associazione, nel trattamento dei tumori solidi	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed <u>Bonadonna G. et al</u> , Medicina Oncologica, Settima Edizione
Interferone alfa 2a	Trattamento del sarcoma di Kaposi non HIV	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed
Irinotecan	Trattamento di seconda linea dei carcinomi avanzati del tratto gastroenterico (colon, retto, esofago, stomaco e pancreas)	<u>Linee guida AIOM-Tumori del colon</u> , edizione 2018 <u>Linee guida AIOM-Tumori dell'esofago</u> , edizione 2018 <u>Linee guida AIOM-Neoplasie dello stomaco e della giunzione esofago-gastrica</u> , edizione 2018 <u>Linee guida AIOM-Carcinoma del pancreas esocrino</u> , edizione 2018
	Trattamento di prima linea del carcinoma del pancreas	<u>Conroy T. et al</u> , FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med 2011

<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
	<p>Trattamento del glioblastoma recidivante a fallimento della terapia con temozolomide</p>	<p><u>Puduvalli V.K. et al</u>, Phase II trial of irinotecan and thalidomide in adults with recurrent glioblastoma multiforme. Neuro Oncol. 2008</p> <p><u>Vredenburgh J.J. et al</u>, Experience with irinotecan for the treatment of malignant glioma. Neuro Oncol. 2009</p> <p><u>Friedman H.S. et al</u>, Irinotecan therapy in adults with recurrent or progressive malignant glioma. J Clin Oncol. 1999</p> <p><u>Weller M. et al</u>, Topoisomerase-1 inhibitors for human malignant gliomas: differential modulation of p53, p21, bax and bcl-2 expression and of CD95-mediated apoptosis by camptothecin and beta-lapachone. Int J Cancer. 1997</p> <p><u>Nakatsu S. et al</u>, Induction of apoptosis in multidrug resistant (MDR) human glioblastoma cells by SN-38, a metabolite of the camptothecin derivative CPT-11. Cancer Chemother Pharmacol. 1997</p> <p><u>Buckner J.C. et al</u>, Irinotecan in the treatment of glioma patients: current and future studies of the North Central Cancer Treatment Group. Cancer. 2003</p> <p><u>Raymond E. et al</u>, Multicentre phase II study and pharmacokinetic analysis of irinotecan in chemotherapy-naïve patients with glioblastoma. Ann Oncol. 2003</p> <p><u>Chamberlain M.C.</u> Salvage chemotherapy with CPT-11 for recurrent glioblastoma multiforme. J Neurooncol. 2002</p> <p><u>Cloughesy T.F. et al</u>, Irinotecan treatment for recurrent malignant glioma using an every-three-week regimen. Am J Clin Oncol. 2002</p> <p><u>Cloughesy T.F. et al</u>, Two studies evaluating irinotecan treatment for recurrent malignant glioma using an every-three-week regimen. Cancer 2003</p> <p><u>Batchelor T.T. et al</u>, Phase 2 study of weekly irinotecan in adults with recurrent malignant glioma: final report of NABTT 97-11. Neuro-Oncol. 2004</p>

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<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
		<p><u>Gilbert M.R. et al</u>, Phase I clinical and pharmacokinetic study of irinotecan in adults with recurrent malignant glioma. Clin Cancer Res 2003</p> <p><u>Prados M.D. et al</u>, Phase 1 trial of irinotecan (CPT-11) in patients with recurrent malignant glioma: a North American Brain Tumor Consortium study. Neuro-Oncol. 2004</p> <p><u>Prados M.D. et al</u>, A phase 2 trial of irinotecan (CPT-11) in patients with recurrent malignant glioma: a North American Brain Tumor Consortium study. Neuro-Oncol. 2006.</p>
	Trattamento di terza linea e oltre dei tumori carcinomi dell'esofago e dello stomaco	<p><u>Pasquini G., et al</u>. Third-Line Chemotherapy with Irinotecan plus 5-Fluorouracil in Caucasian Metastatic Gastric Cancer Patients. Oncology. 2016; 91(6):311-316.</p>

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<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
	<p>Trattamento di seconda linea del carcinoma avanzato delle vie biliari</p>	<p><u>Larsen FO, Markussen A, Diness LV, Nielsen D.</u> Efficacy and Safety of Capecitabine, Irinotecan, Gemcitabine, and Bevacizumab as Second-Line Treatment in Advanced Biliary Tract Cancer: A Phase II Study. <i>Oncology</i>. 2018; 94(1): 19-24.</p> <p><u>Zheng Y et al.</u> A randomised phase II study of second-line XELIRI regimen versus irinotecan monotherapy in advanced biliary tract cancer patients progressed on gemcitabine and cisplatin. <i>Br J Cancer</i>. 2018; 119(3): 291-295.</p>
	<p>Trattamento del carcinoma del pancreas resecato o non resecabile</p>	<p><u>Conroy T. et al.</u> FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer. <i>N Engl J Med</i>. 2018; 379(25): 2395-2406.</p> <p><u>Suker M, et al.</u> FOLFIRINOX for locally advanced pancreatic cancer: a systematic review and patient-level meta-analysis. <i>Lancet Oncol</i>. 2016; 17(6): 801-10.</p>

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<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
	Trattamento dell'adenocarcinoma del colon metastatico in pazienti in progressione dopo precedente terapia con irinotecan e/o precedentemente trattati con irinotecan senza progressione	<u>Labianca R et al.</u> Intermittent versus continuous chemotherapy in advanced colorectal cancer: a randomised 'GISCAD' trial. Ann Oncol. 2011; 22(5):1236-42.
Lanreotide acetato	Trattamento di tumori neuroendocrini in fase evolutiva in pazienti non sindromici	<u>Linee guida AIOM-Neoplasie neuroendocrine</u> , edizione 2018

Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
<p>Letrozolo</p>	<p>Trattamento del tumore della mammella maschile in fase avanzata, in associazione a LHRH analogo, in caso di fallimento di tamoxifen o intolleranza a tale farmaco (Si intende autorizzato lo schema terapeutico dell'associazione)</p>	<p><u>White J. et al</u>, Male breast carcinoma: increased awareness needed. Breast Cancer Research, 2011</p> <p><u>Cardoso F. et al</u>, 1st international consensus guideline for advanced breast cancer (ABC 1). Breast 2012</p> <p><u>Korde L.A. et al</u>, Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol 2010</p> <p><u>Giordano S.H., Hortobagay GN.</u> Leuprolide acetate plus aromatase inhibition for male breast cancer. J Clin Oncol 2006</p> <p><u>Linee guida AIOM-Neoplasie della mammella</u>, edizione 2017</p>
	<p>In monoterapia nel trattamento del carcinoma ovarico recidivato</p>	<p><u>Rao G.G. et al</u>, Hormonal therapy in epithelial ovarian cancer. Expert Rev Anticancer Ther 2006</p> <p><u>Papadimitriou C.A. et al</u>, Hormonal therapy with letrozole for relapsed epithelial ovarian cancer. Long-term results of a phase II study. Oncology 2004</p> <p><u>Bowman A. et al</u>, CA125 response is associated with estrogen receptor expression in a phase II trial of letrozole in ovarian cancer: identification of an endocrine-sensitive subgroup. Clin Cancer Res 2002</p> <p><u>del Carmen M.G. et al</u>, Phase II trial of anastrozole in women with asymptomatic mullerian cancer. Gynecol Oncol 2003</p> <p><u>Ramirez P.T. et al</u>, Efficacy of letrozole in the treatment of recurrent platinum- and taxane-resistant high-grade cancer of the ovary or peritoneum. Gynecol Oncol 2008</p> <p><u>Serkies K. et al</u>, The role of hormonal factors and endocrine therapy in ovarian cancer. Współczesna Onkologia/Contemporary Oncology 2013</p> <p><u>NCCN Clinical Practice Guidelines in Oncology- Ovarian Cancer</u>, version</p>

Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	<p>In associazione a LHRH analogo nel trattamento di pazienti in premenopausa con carcinoma mammario metastatico e recettori ormonali positivi (nei casi con accertata controindicazione a tamoxifene)</p>	<p>2.2018</p> <p>Park I.H. et al, Phase II parallel group study showing comparable efficacy between premenopausal metastatic breast cancer patients treated with letrozole plus goserelin and postmenopausal patients treated with letrozole alone as first-line hormone therapy. J Clin Oncol. 2010</p>
<p>Medrossiprogesterone acetato</p>	<p>Trattamento del tumore della mammella maschile</p>	<p><u>DeVita V.T. et al</u>, Cancer: Principles and Practice of Oncology, 6th Ed <u>Bonadonna G. et al</u>, Medicina Oncologica, Settima Edizione</p>
<p>Megestrol Acetato</p>	<p>Trattamento del tumore della mammella maschile</p>	<p><u>DeVita V.T. et al</u>, Cancer: Principles and Practice of Oncology, 6th Ed <u>Bonadonna G. et al</u>, Medicina Oncologica, Settima Edizione</p>
<p>Micofenolato mofetile</p>	<p>Trattamento di malattie autoimmuni non rispondenti a terapie standard, sindrome nefrosica steroide-resistente e steroide-dipendente, trapianto di midollo osseo</p>	<p><u>Tannuri U. et al</u>, Mycophenolate mofetil promotes prolonged improvement of renal dysfunction after pediatric liver transplantation: experience of a single center. Pediatr Transplant. 2007 <u>Vilalta Casas R. et al</u>, Mycophenolic Acid reaches therapeutic levels whereas mycophenolate mofetil does not. Transplant Proc. 2006 <u>Fujinaga S. et al</u>, A prospective study on the use of mycophenolate mofetil in children with cyclosporine-dependent nephrotic syndrome. Pediatr Nephrol. 2007 <u>Ksiazek J. et al</u>, Evaluation of arterial intima-media thickness (IMT) in children with idiopathic nephrotic syndrome--preliminary report. Przegl</p>

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Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
		Lek. 2006. <u>Kwinta-Rybicka J. et al</u> , Mycophenolate mofetil in treatment of childhood nephrotic syndrome--preliminary report. Przegl Lek. 2006
Micofenolato sodico	Trattamento di malattie autoimmuni gravi in pazienti in cui il trattamento con micofenolato mofetile sia associato a effetti collaterali di tipo gastroenterico che richiedano la diminuzione/sospensione della dose	Behrend M. et al, Enteric-coated mycophenolate sodium: tolerability profile compared with mycophenolate mofetil. Drugs 2005
Mitomicina C	In monoterapia o in associazione nel trattamento dei tumori solidi e in particolare del carcinoma dell'ano	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed <u>Bonadonna G. et al</u> , Medicina Oncologica, Settima Edizione <u>Linee guida AIOM- Neoplasie del retto e ano</u> , edizione 2017
Nab-paclitaxel	Somministrazione con schedula settimanale nel trattamento del carcinoma mammario avanzato	<u>Gradishar W.J. et al</u> , Phase II trial of nab-paclitaxel compared with docetaxel as first-line chemotherapy in patients with metastatic breast cancer: final analysis of overall survival. Clin Breast Cancer 2012
Octreotide	Trattamento di tumori neuroendocrini in fase evolutiva in pazienti non sindromici	<u>Linee guida AIOM-Neoplasie neuroendocrine</u> , edizione 2018

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Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	<p>Gestione della diarrea indotta da chemioterapia e resistente a trattamento con loperamide</p>	<p><u>Topkan E. et al</u>, Octreotide in the management of chemoradiotherapy induced diarrhea refractory to loperamide in patients with rectal carcinoma. Oncology 2006</p> <p><u>Wadler S. et al</u>, Recommended guidelines for the treatment of chemotherapy-induced diarrhea. J Clin Oncol 1998</p>
<p>Octreotide acetato</p>	<p>Trattamento di tumori neuroendocrini in fase evolutiva in pazienti non sindromici</p>	<p><u>Linee guida AIOM</u>-Neoplasie neuroendocrine, edizione 2018</p>
<p>Oxaliplatino</p>	<p>In associazione a farmaci alternativi al fluorouracile nel trattamento del tumore metastatico del colon-retto</p>	<p><u>Linee guida AIOM</u>- Tumori del colon, edizione 2018</p>
	<p>In associazione a gemcitabina nel trattamento del carcinoma del pancreas e delle vie biliari</p>	<p><u>Louvet C. et al</u>, Gemcitabine in combination with oxaliplatin compared with gemcitabine alone in locally advanced or metastatic pancreatic cancer: results of a GERCOR and GISCAD phase III trial. J Clin Oncol 2005</p> <p><u>Linee guida AIOM</u>- Tumori delle vie biliari, edizione 2018</p>

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Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	<p>Con fluoropirimidine o raltitrexed in associazione ad antracicline o docetaxel nel trattamento del carcinoma gastrico avanzato o metastatico</p>	<p><u>Seo H.Y. et al</u>, Treatment outcomes of oxaliplatin, 5-FU, and leucovorin as salvage therapy for patients with advanced or metastatic gastric cancer: a retrospective analysis. Cancer Chemother Pharmacol. 2008</p> <p><u>Luo H.Y. et al</u>, A Pilot Study of oxaliplatin, fluorouracil and folinic acid (FOLFOX-6) as first-line chemotherapy in advanced or recurrent gastric Cancer. Chemotherapy. 2008</p> <p><u>Liu Z.F. et al</u>, Biweekly oxaliplatin in combination with continuous infusional 5-fluorouracil and leucovorin (modified FOLFOX-4 regimen) as first-line chemotherapy for elderly patients with advanced gastric cancer. Am J Clin Oncol. 2008</p> <p><u>Hwang W.S. et al</u>, Phase II study of oxaliplatin in combination with continuous infusion of 5- fluorouracil/leucovorin as first-line chemotherapy in patients with advanced gastric cancer. Anticancer Drugs. 2008</p> <p><u>Jeong J. et al</u>, Phase II study of combination chemotherapy of 5-fluorouracil, low-dose leucovorin, and oxaliplatin (FLOX regimen) in pretreated advanced gastric cancer. Ann Oncol 2008</p> <p><u>Jatoi A. et al</u>, Oxaliplatin and capecitabine in patients with metastatic adenocarcinoma of the esophagus, gastroesophageal junction and gastric cardia: a phase II study from the North Central Cancer Treatment Group Ann Oncol. 2006</p> <p><u>Kim D.Y. et al</u>, Phase II study of oxaliplatin, 5-fluorouracil and leucovorin in previously platinum-treated patients with advanced gastric cancer. Ann Oncol. 2003</p> <p><u>Keam B. et al</u>, Modified FOLFOX-6 chemotherapy in advanced gastric cancer: Results of phase II study and comprehensive analysis of polymorphisms as a predictive and prognostic marker. BMC Cancer 2008</p> <p><u>Zhu X. et al</u>, Phase II clinical trial of advanced and metastatic gastric</p>

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<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
		<p>cancer based on continuous infusion of 5-fluorouracil combined with epirubicin and oxaliplatin. J Cancer Res Clin Oncol. 2008</p> <p><u>Zhu X. et al</u>, Epirubicin combined with oxaliplatin and 5-day continuous infusion of 5-fluorouracil as a first-line treatment for metastatic gastric cancer: treatment outcomes and analysis of prognostic factors. J Cancer Res Clin Oncol. 2015</p> <p><u>Barone C. et al</u>, Docetaxel and oxaliplatin combination in second-line treatment of patients with advanced gastric cancer. Gastric Cancer 2007</p> <p><u>Neri B. et al</u>, Oxaliplatin, 5-fluorouracil/leucovorin and epirubicin as first-line treatment in advanced gastric carcinoma: a phase II study. Br J Cancer 2007</p> <p><u>Al-Batran S.E. et al</u>, Biweekly fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) for patients with metastatic adenocarcinoma of the stomach or esophagogastric junction: a phase II trial of the Arbeitsgemeinschaft Internistische Onkologie. Ann Oncol 2008</p> <p><u>Schmid K.E. et al</u>, Second-line treatment of advanced gastric cancer with oxaliplatin plus raltitrexed. Onkologie. 2003</p>

Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	<p>In associazione a fluoropirimidine, anche senza antracicline o taxani, nel trattamento del carcinoma gastrico in fase adiuvante o neoadiuvante e nella malattia avanzata</p>	<p><u>Cunningham D. et al</u>, Capecitabine and oxaliplatin for advanced esophagogastric cancer. N Engl J Med. 2008</p> <p><u>Al-Batran S.E. et al</u>, Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J of Clinical Oncol 2008</p> <p><u>Montagnani F. et al</u>, Effectiveness and safety of oxaliplatin compared to cisplatin for advanced, unresectable gastric cancer: a systematic review and meta-analysis. Gastric Cancer 2014</p> <p><u>Noh S.H. et al</u>, Adjuvant capecitabine plus oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): 5-year follow-up of an open-label, randomised phase 3 trial. Lancet Oncol 2014</p> <p><u>Al-Batran S.E. et al</u>, Histopathological regression after neoadjuvant docetaxel, oxaliplatin, fluorouracil, and leucovorin versus epirubicin, cisplatin, and fluorouracil or capecitabine in patients with resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4-AIO): results from the phase 2 part of a multicentre, open-label, randomised phase 2/3 trial. Lancet Oncol 2016</p> <p><u>Al-Batran S.E. et al</u>, Perioperative chemotherapy with docetaxel, oxaliplatin, and fluorouracil/leucovorin (HOT) versus epirubicin, cisplatin, and fluorouracil or capecitabine (ECF/ECX) for resectable gastric or gastroesophageal junction adenocarcinoma (FLOT4-AIO): a multi center randomized phase 3 trial. Abstract 4004 ASCO 2017</p>

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Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	<p>Terapia di salvataggio dei tumori germinali testicolari ed extragonadici, in associazione a gemcitabina o a gemcitabina e paclitaxel</p>	<p><u>Bokemeyer C. et al</u>, Combination chemotherapy with gemcitabine, oxaliplatin, and paclitaxel in patients with cisplatin-refractory or multiply relapsed germ-cell tumors: a study of the German Testicular Cancer Study Group. Ann Oncol. 2008</p> <p><u>De Giorgi U. et al</u>, Phase II study of oxaliplatin and gemcitabine salvage chemotherapy in patients with cisplatin-refractory nonseminomatous germ cell tumor. Eur Urol. 2006</p> <p><u>Kollmannsberger C. et al</u>, Combination chemotherapy with gemcitabine plus oxaliplatin in patients with intensively pretreated or refractory germ cell cancer: a study of the German Testicular Cancer Study Group. J Clin Oncol 2004</p> <p><u>Kollmannsberger C. et al</u>, Combination chemotherapy with gemcitabine, oxaliplatin, and paclitaxel in patients with cisplatin-refractory or multiply relapsed germ-cell tumors: a study of the German Testicular Cancer Study Group. Ann Oncol 2008</p> <p><u>Pectasides D. et al</u>, Gemcitabine and oxaliplatin (GEMOX) in patients with cisplatin-refractory germ cell tumors: a phase II study. Ann Oncol 2004</p>
	<p>Trattamento di prima linea del carcinoma del pancreas (anche non associato a gemcitabina)</p>	<p><u>Conroy T. et al</u>, FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med 2011</p> <p><u>Linee guida AIOM</u>- Carcinoma del pancreas esocrino, edizione 2018</p>

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Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	Trattamento di seconda linea del carcinoma del pancreas	<u>Oettle H. et al.</u> , Second-line oxaliplatin, folinic acid, and fluorouracil versus folinic acid and fluorouracil alone for gemcitabine refractory pancreatic cancer: Outcomes from the CONKO-003 trial. J Clin Oncol 2014
	Trattamento adiuvante e neoadiuvante del carcinoma gastrico e della giunzione gastro-esofagea	<u>Bang Y-W, et al.</u> Adjuvant capecitabine and oxaliplatin for gastric cancer, after D2 gastrectomy (CLASSIC) a phase 3 open-label, randomized controlled trial. Lancet. 2012; 379 (9813): 315-21. <u>Al-Batran S, et al.</u> Histopathological regression after neoadjuvant docetaxel, oxaliplatin, fluorouracil, and leucovorin versus epirubicin, cisplatin, and fluorouracil or capecitabine in patients with resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4-AIO): results from the phase 2 part of a multicentre, open-label, randomised phase 2/3 trial. Lancet Oncol. 2016; 17(12): 1697-1708.
	Trattamento del carcinoma del pancreas resecato o non resecabile	<u>Conroy T. et al.</u> FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer. N Engl J Med. 2018; 379(25): 2395-2406. <u>Suker M, et al.</u> FOLFIRINOX for locally advanced pancreatic cancer: a systematic review and patient-level meta-analysis. Lancet Oncol. 2016; 17(6): 801-10.
	Trattamento dei tumori delle vie biliari anche non associato a gemcitabina	<u>Schinzari G, et al.</u> First-line Treatment of Advanced Biliary Ducts Carcinoma: A Randomized Phase II Study Evaluating 5-FU/LV Plus Oxaliplatin (Folfox 4) Versus 5-FU/LV (de Gramont Regimen). Anticancer Res. 2017; 37(9): 5193-5197.

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Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	Trattamento dei tumori neuroendocrini avanzati	<u>Spada F. et al</u> Oxaliplatin-Based Chemotherapy in Advanced Neuroendocrine Tumors: Clinical Outcomes and Preliminary Correlation with Biological Factors. Neuroendocrinology. 2016; 103(6): 806-14.
Paclitaxel	Trattamento del carcinoma avanzato del distretto cervico-facciale.	<u>Linee guida AIOM</u> - Tumori della Testa e del Collo, edizione 2018
	In combinazione con radioterapia per il trattamento del tumore di esofago/giunzione gastroesofagea/cardias	<u>Van Hagen P. et al</u> , Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med. 2012.
	Utilizzo nel carcinoma dell'endometrio e nel carcinoma metastatico della cervice	<u>Linee guida AIOM</u> - Neoplasie dell'utero: endometrio e cervice, edizione 2018
	Utilizzo nella neoplasia germinale del testicolo	<u>Linee guida AIOM</u> - Tumori del testicolo, edizione 2018

<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
	Utilizzo nel carcinoma della vescica	<u>Linee guida AIOM</u> - Tumori dell'urotelio, edizione 2018
	Utilizzo nei sarcomi dei tessuti molli	<u>Linee guida AIOM</u> - Sarcomi dei tessuti molli, edizione 2018
	Trattamento del melanoma metastatico pretrattato	<p><u>Gogas H.</u> The role of taxanes in the treatment of metastatic melanoma. Melanoma Res 2004;14:415-420</p> <p><u>Zonder JA.</u> Phase II trial of weekly paclitaxel as 2nd line treatment of metastatic malignant melanoma (MMM). Proc Am Soc Clin Oncol 2000; 19:(abstract 2249]</p> <p><u>Bedikian AY.</u> Phase II evaluation of paclitaxel by short iv infusion in metastatic melanoma. Melanoma Res 2004;14:63-67.</p>
	Trattamento del carcinoma ovarico in prima linea ovvero in adiuvante nei primi stadi a rischio, in associazione a carboplatino	<p><u>DuBois A. et al,</u> A randomized clinical trial of cisplatin/ paclitaxel vs carboplatin/paclitaxel as first line treatment of ovarian cancer. J Natl Cancer Inst 2003</p> <p><u>Colombo N. et al,</u> International Collaborative ovarian neoplasms trial 1: a randomized trial of adjuvant chemotherapy in women with early stage ovarian cancer J Natl cancer Inst 2003</p>
	Trattamento del tumore della mammella in associazione ad antracicline, seguita da terapia sequenziale con ciclofosfamide, metotrexate e fluorouracile, in fase adiuvante, in pazienti con	<p><u>Bonadonna G. et al,</u> Medicina Oncologica, Settima Edizione</p> <p><u>Gianni L. et al,</u> Feasibility and tolerability of sequential doxorubicin/paclitaxel followed by cyclophosphamide, methotrexate, and fluorouracil and its effects on tumor response as preoperative</p>

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Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	linfonodi positivi o negativi ad alto rischio, e in fase neoadiuvante	therapy Clin Cancer Res. 2005 <u>Battelli N. et al</u> , Paclitaxel and epirubicin followed by cyclophosphamide, methotrexate and 5-fluorouracil for patients with stage IIIC breast cancer with ten or more involved axillary lymph nodes. Am J Clin Oncol 2006
	Somministrazione settimanale in adiuvante nel trattamento del carcinoma della mammella con linfonodi positivi o negativi a rischio	<u>Sparano J.A. et al</u> , Weekly paclitaxel in the adjuvant treatment of breast cancer. N Engl J Med. 2008 <u>Martin M. et al</u> , Randomized phase 3 trial of fluorouracil, epirubicin and cyclophosphamide alone or followed by paclitaxel for early breast cancer. J Natl Cancer Inst 2008
	Somministrazione settimanale in adiuvante in combinazione con trastuzumab (originatore o biosimilare) nel trattamento del carcinoma della mammella fino a 3 cm, N0, HER2-positivo	<u>Tolaney S.M. et al</u> . Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer. N Engl J Med 2015
	Somministrazione settimanale nel trattamento del carcinoma metastatico della mammella HER2-negativo	<u>Sparano J.A. et al</u> , Weekly paclitaxel in the adjuvant treatment of breast cancer. N Engl J Med 2008 <u>Linee guida AIOM- Neoplasie della mammella, edizione 2018</u>
	In associazione a trastuzumab, nel trattamento del carcinoma mammario metastatico HER2-positivo in linee successive alla prima	<u>Cardoso F, Bedard PL, Winer EP et ESO-MBC Task Force</u> : International guidelines for management of metastatic breast cancer: combination vs sequential single-agent chemotherapy. J Natl Cancer Inst Sep 2;101(17):1174-1181,2009. <u>Oostendorp LJ, Stalmeier PF, Donders AR et al</u> : Efficacy and safety of palliative chemotherapy for patients with advanced breast cancer pretreated with anthracyclines and taxanes: a systematic review. Lancet Oncol Oct;12(11):1053-1061,2011. <u>Puglisi F, Rea D, Kroes MA et al</u> : Second-line single-agent chemotherapy

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		<p>in human epidermal growth factor receptor 2-negative metastatic breast cancer: A systematic review. <i>Cancer Treat Rev</i> Feb;43:36-49, 2016.</p> <p><u>Linee guida AIOM</u>- Neoplasie della mammella, edizione 2018</p>
	<p>In monoterapia o in associazione nel trattamento del carcinoma avanzato del polmone a piccole o a grandi cellule</p>	<p><u>Ceresoli G.L. et al</u>, Phase II study of weekly paclitaxel as second-line therapy in patients with advanced non-small cell lung cancer. <i>Lung Cancer</i> 2004</p> <p><u>Smit E.F. et al</u>, A phase II study of paclitaxel in heavily pretreated patients with small-cell lung cancer. <i>Br J Cancer</i> 1998</p>
	<p>In monoterapia, come trattamento di seconda linea del carcinoma gastrico e della giunzione gastroesofagea avanzato</p>	<p><u>Hironaka S. et al</u>, Weekly paclitaxel as second-line chemotherapy for advanced or recurrent gastric cancer. <i>Gastric Cancer</i> 2006.</p> <p><u>Kadokura M. et al</u>, Weekly paclitaxel as second-line chemotherapy in Japanese patients with advanced gastric cancer. <i>Anticancer Res</i> 2013.</p>
	<p>In monoterapia, nel trattamento di seconda linea del carcinoma gastrico avanzato.</p>	<p><u>Kodera Y, et al</u>. A phase II study of weekly paclitaxel as second line chemotherapy for advanced or recurrent gastric, (CCOG0302 study). <i>Anticancer Res</i> 2007; 27 (4C): 2667-71.</p> <p><u>Hironaka S. et al</u>. Weekly paclitaxel as second-line chemotherapy for advanced or recurrent gastric cancer. <i>Gastric Cancer</i>. 2006;9(1):14-8.</p>
	<p>In associazione a ramucirumab, nel trattamento di seconda linea del carcinoma gastrico avanzato</p>	<p><u>Wilke H, et al</u>. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase III trial. <i>Lancet Oncol</i>. 2014; 15 (11): 1224-35.</p>
	<p>In monoterapia o in combinazione, nel trattamento del tumore del polmone a piccole</p>	<p><u>Ceresoli GL, Dell'Oro S, Passoni P, Villa E</u>. Phase II study of paclitaxel and epirubicin as first line treatment in patients with metastatic nonsmall</p>

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	cellule	cell lung carcinoma. Cancer. 2000; 89(1): 89-96. <u>Yamamoto N, et al.</u> Phase II study of weekly paclitaxel for relapsed and refractory small cell lung cancer. Anticancer Res. 2006; 26(1B):777-81.
	Trattamento dei tumori epiteliali del timo	<u>Lemma GL. et al.</u> Phase II study of carboplatin and paclitaxel in advanced thymoma and thymic carcinoma. J Clin Oncol. 2011; 29 (15): 2060-5.
	Trattamento del carcinoma squamoso dell'esofago, dell'adenocarcinoma dell'esofago e del cardias localmente avanzati	<u>Van Hagen P, et al.</u> "Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med. 2012; 366 (22): 2074-84.
Pemetrexed	Trattamento del mesotelioma peritoneale, in prima linea in associazione a sali di platino, o in linea successiva in monoterapia, laddove non precedentemente utilizzato	<u>Mirarabshahii P. et al.</u> Diffuse malignant peritoneal mesothelioma – An update on treatment. Cancer Treatment Reviews 2012 <u>Fasola G. et al.</u> Dramatic tumour response to pemetrexed single-agent in an elderly patient with malignant peritoneal mesothelioma: a case report. BMC Cancer 2006 <u>Vogelzang N.J. et al.</u> Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol 2003 <u>Jänne P.A. et al.</u> Open label study of pemetrexed alone or in combination with cisplatin for the treatment of patients with peritoneal mesothelioma: outcomes of an expanded access program. Clin Lung Cancer 2005 <u>Carteni G. et al,</u> Malignant peritoneal mesothelioma – results from the International Expanded Access Program using pemetrexed alone or in combination with a platinum agent. Lung Cancer 2009

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Procarbazina	In combinazione con altri farmaci nel trattamento delle neoplasie cerebrali e dei linfomi non Hodgkin	<u>DeVita V.T. et al</u> , Cancer: Principles and Practice of Oncology, 6 th Ed <u>Bonadonna G. et al</u> , Medicina Oncologica, Settima Edizione
Raltitrexed	Trattamento del mesotelioma peritoneale, in prima linea in associazione a sali di platino, o in linea successiva in monoterapia, laddove non precedentemente utilizzato	<u>Mirarabshahii P. et al</u> , Diffuse malignant peritoneal mesothelioma – An update on treatment. Cancer Treatment Reviews 2012 <u>Garcia-Carbonero R. et al</u> , Systemic chemotherapy in the management of malignant peritoneal mesothelioma. Eur J Surg Oncol 2006 <u>Fizazi K. et al</u> , Combination of raltitrexed and oxaliplatin is an active regimen in malignant mesothelioma: results of a phase II study. J Clin Oncol. 2003
Tamoxifene	Trattamento del tumore della mammella maschile	Linee guida AIOM- Neoplasie della mammella, edizione 2018
	Trattamento della fibromatosi aggressiva	DeVita V.T. et al, Cancer: Principles and Practice of Oncology, 6th Ed Bonadonna G. et al, Medicina Oncologica, Settima Edizione
	In monoterapia nel trattamento del carcinoma ovarico recidivato	NCCN Clinical Practice Guidelines in Oncology-Ovarian Cancer, version 2.2018
Tegafur/Uracile	In alternativa al fluorouracile dove non si ritenga opportuno o indicato un trattamento infusioneale	Chionh F. et al, Oral versus intravenous fluoropyrimidines for colorectal cancer. Cochrane Database Syst Rev 2017
Temozolomide	Trattamento del melanoma maligno quando non si ritenga opportuno un trattamento con dacarbazina	Linee guida AIOM- Melanoma, edizione 2018

<i>Nome principio attivo</i>	<i>Indicazione terapeutica off-label</i>	<i>Referenze di letteratura</i>
	<p>In associazione a radioterapia encefalica nel trattamento delle metastasi cerebrali da neoplasia polmonare e mammaria</p>	<p><u>Christodoulou C. et al</u>, Phase II study of temozolomide in heavily pretreated cancer patients with brain metastases. Ann Oncol 2001</p> <p><u>Abrey L.E. et al</u>, A phase II trial of temozolomide for patients with recurrent or progressive brain metastases. J Neurooncol 2001</p> <p><u>Antonadau D. et al</u>, Phase II randomised trial of temozolomide and concurrent radiotherapy in patients with brain metastases. J Clin Oncol 2002</p> <p><u>Verger E. et al</u>, Temozolomide and concomitant whole brain radiotherapy in patients with brain metastases: a phase II randomized trial. Int J Radiat Oncol Biol Phys 2005</p> <p><u>Addeo R. et al</u>, Concomitant treatment of brain metastasis with Whole Brain Radiotherapy [WBRT] and Temozolomide [TMZ] is active and improves Quality of Life. BMC Cancer 2007</p> <p><u>Addeo R. et al</u>, Phase II Trial of temozolomide using protracted low dose and whole brain radiotherapy for non-small-cell lung cancer and breast cancer patients with brain metastases. Cancer 2008</p> <p><u>Eichler A.F. et al</u>, Multidisciplinary management of brain metastases. Oncologist 2007</p>
	<p>Trattamento degli adenomi ipofisari aggressivi o carcinomi ipofisari</p>	<p><u>Syro L.V. et al</u>, Treatment of pituitary neoplasms with temozolomide: a review. Cancer 2010</p> <p><u>Raverot G. et al</u>, Temozolomide treatment in aggressive pituitary tumors and pituitary carcinomas: a French multicenter experience. J Clin Endocrinol Metab 2010</p> <p><u>Hagen C. et al</u>, Temozolomide treatment of a pituitary carcinoma and two pituitary macroadenomas resistant to conventional therapy. Eur J Endocrinol 2009</p> <p><u>Byrne S. et al</u>, A novel use of temozolomide in a patient with malignant prolactinoma. J Clin Neurosci 2009</p>

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		<p><u>Syro L.V. et al</u>, Effect of temozolomide in a patient with recurring oncocyctic gonadotrophic pituitary adenoma. Hormones (Athens) 2009</p>
	<p>Trattamento dei carcinomi endocrini avanzati, qualora non si ritenga di praticare streptozotocina</p>	<p><u>Ekeblad S. et al</u>, Temozolomide as monotherapy is effective in treatment of advanced malignant neuroendocrine tumors. Clin Cancer Res 2007</p> <p><u>Maire F. et al</u>, Temozolomide: a safe and effective treatment for malignant digestive neuroendocrine tumors. Neuroendocrinology 2009</p>
<p>Trastuzumab (originatore o biosimilare)</p>	<p>Trattamento del tumore metastatico della mammella HER2 positivo o in progressione, in associazione a vinorelbina o capecitabina</p>	<p><u>Bartsch R. et al</u>, Analysis of trastuzumab and chemotherapy in advanced breast cancer after the failure of at least one earlier combination: an observational study. BMC Cancer 2006</p> <p><u>Garcia Saenz J.A. et al</u>, Trastuzumab associated with successive cytotoxic therapies beyond disease progression in metastatic breast cancer. Clin Breast Cancer 2005</p> <p><u>Fountzilas G. et al</u>, Continuation of trastuzumab beyond disease progression is feasible and safe in patients with metastatic breast cancer: a retrospective analysis of 80 cases by the hellenic cooperative oncology group. Clin Breast Cancer 2003</p> <p><u>Adamo V. et al</u>, Safety and activity of trastuzumab-containing therapies for the treatment of metastatic breast cancer: our long-term clinical experience (GOIM study). Ann Oncol 2007</p> <p><u>Tripathy D. et al</u>, Safety of treatment of metastatic breast cancer with trastuzumab beyond disease progression J Clin Oncol 2004</p>

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	<p>Trattamento del carcinoma mammario metastatico HER2-positivo in linee successive alla prima, in associazione o meno ad altri chemioterapici o trattamenti ormonali in pazienti già trattati con trastuzumab o altri farmaci anti-HER2.</p>	<p><u>Von Minckwitz G, du Bois A, Schmidt M et al: Trastuzumab beyond progression in human epidermal growth factor receptor 2-positive advanced breast cancer: a German Breast Group 26/Breast International Group 03-05 study.</u> J Clin Oncol, Apr 20;27(12):1999-2006, 2009</p> <p>Blackwell KL, Burstein HJ, Storniolo AM et al.: <i>Overall survival benefit with lapatinib in combination with trastuzumab for patients with human epidermal growth factor receptor 2 positive metastatic breast cancer: final results from the EGF104900 Study.</i> J Clin Oncol, Jul 20;30(21):2585-2592, 2012</p> <p><u>Verma S, Miles D, Gianni L et EMILIA Study Group.</u>Trastuzumab emtansine for HER2-positive advanced breast cancer. N Engl J Med. 2012 Nov 8;367(19):1783-1791, 2012</p> <p><u>Cardoso F, Bedard PL, Winer EP et ESO-MBC Task Force: International guidelines for management of metastatic breast cancer: combination vs sequential single-agent chemotherapy.</u> J Natl Cancer Inst Sep 2;101(17):1174-1181,2009</p> <p><u>Linee guida AIOM- Neoplasie della mammella, edizione 2018.</u></p>
<p>Vinblastina</p>	<p>Trattamento del carcinomi della vescica e del rene</p>	<p><u>DeVita V.T. et al, Cancer: Principles and Practice of Oncology, 6th Ed</u> <u>Bonadonna G. et al, Medicina Oncologica, Settima Edizione</u></p>
<p>Vinorelbina</p>	<p>Trattamento del carcinoma mammario metastatico HER2 positivo (IHC 3+ o FISH positivo) in associazione a trastuzumab (originatore o biosimilare) in pazienti precedentemente trattate con taxani in adiuvante o non candidate al trattamento con taxani</p>	<p><u>NCCN Clinical Practice Guidelines in Oncology-Breast Cancer, version 1.2018</u></p>

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Nome principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
	Trattamento del carcinoma del distretto cervico facciale	<u>Chan A.T.C. et al</u> , Nasopharyngeal cancer: EHNS-ESMO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2012
	Trattamento del carcinoma prostatico ormonoresistente	<u>NCCN Clinical Practice Guidelines in Oncology-Prostate Cancer</u> , version 2.2018
	Trattamento del carcinoma della cervice uterina.	<u>Linee guida AIOM- Neoplasie dell'utero: endometrio e cervice</u> , edizione 2017
	Trattamento del carcinoma dell'ovaio pluritrattato in progressione	<u>NCCN Clinical Practice Guidelines in Oncology-Ovarian Cancer</u> , version 2.2018
	Somministrazione per via orale nelle stesse indicazioni della formulazione endovenosa	<p><u>Caristi N. et al</u>, Oral vinorelbine as first line chemotherapy in unfit elderly patients with hormone-refractory prostate cancer. J Chemother 2008</p> <p><u>Jensen L.H. et al</u>, Randomized cross-over study of patient preference for oral or intravenous vinorelbine in combination with carboplatin in the treatment of advanced NSCLC. Lung Cancer 2008</p> <p><u>Ardizzoia A. et al</u>, Epirubicin-vinorelbine intravenous combination followed by oral vinorelbine as first-line treatment in metastatic breast cancer. Tumori 2007</p> <p><u>Serin D. et al</u>, Vinorelbine alternating oral and intravenous plus epirubicin in first-line therapy of metastatic breast cancer: results of a</p>

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		multicentre phase II study. Br J Cancer 2005
	<p>Trattamento dei tumori solidi con somministrazione settimanale frazionata (metronomica)</p>	<p><u>Briasoulis E. et al</u>, Dose-ranging study of metronomic oral vinorelbine in patients with advanced refractory cancer. Clin Cancer Res 2009</p> <p><u>Briasoulis E. et al</u>, Dose selection trial of metronomic oral vinorelbine monotherapy in patients with metastatic cancer: a hellenic cooperative oncology group clinical translational study. BMC Cancer 2013</p> <p><u>Rajdev L. et al</u>, Phase I trial of metronomic oral vinorelbine in patients with advanced cancer. Cancer Chemother Pharmacol 2011</p> <p><u>Addeo R. et al</u>, Low-dose metronomic oral administration of vinorelbine in the first-line treatment of elderly patients with metastatic breast cancer. Clin Breast Cancer 2010</p> <p><u>De Iuliis F. et al</u>, On and off metronomic oral vinorelbine in elderly women with advanced breast cancer. Tumori 2015</p> <p><u>Camerini A. et al</u>, Metronomic oral vinorelbine as first-line treatment in elderly patients with advanced non-small cell lung cancer: results of a phase II trial (MOVE trial). BMC Cancer 2015</p>
	<p>Trattamento di seconda linea del mesotelioma pleurico maligno pretrattato</p>	<p><u>Steele JP et al</u>. Phase II study of vinorelbine in patients with malignant pleural mesothelioma. J Clin Oncol. 2000; 18(23): 3912-7.</p>