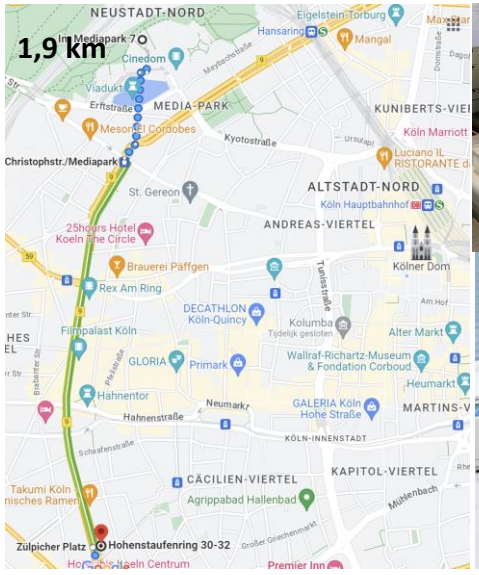
Multiphase combined treatment for adults with GBM, including individualized multimodal immunotherapy:

Single institute real world medical data in the light of clinical trial research data

Stefaan W. Van Gool, Peter Van de Vliet, Linde Kampers, Jennifer Kosmal,
Tobias Sprenger, Volker Schirrmacher, Wilfried Stücker



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Bezirksregierung Köln

HERSTELLUNGSERLAUBNIS

1. Nummer der Erlaubnis/Aktenzeichen	DE_NW_04_MIA_2020_0017
2. Name des Erlaubnisinhabers	Immunologisches und onkologisches Zentrum Köln GmbH & Co. KG
3. Anschrift/en der Betriebsstätte/n des Herstellers / des Einführers	IOZK Laboratorium GmbH Mauritiuswall 48 50676 Köln Immunologisches Onkologisches Zentrum Köln Hohenstaufenring 30-32 50674 Köln
4. Eingetragene Anschrift des Erlaubnisinhabers	Hohenstaufenring 30-32 50674 Köln
5. Umfang der Erlaubnis sowie Darreichungsformen	ANLAGE 1 und ANLAGE 2
6. Rechtsgrundlage der Erlaubniserteilung	§ 13 Absatz 1 des Gesetzes über den Verkehr mit Arzneimitteln (Arzneimittelgesetz - AMG) in gültiger Fassung
7. Name des verantwortlichen Bearbeiters der zuständigen Behörde des Mitgliedstaates, der die Erlaubnis erteilt	Astrid Meiser
8. Unterschrift	Im Auftrag
9. Datum	20.05.2020

Bezirksregierung 170 Köln

DE_NW_04_MIA_2020_0017 Seite 1 von 7 20.05.2020 10:57:52

cancers

MDPI

Article

Individualized Multimodal Immunotherapy for Adults with IDH1 Wild-Type GBM: A Single Institute Experience

Stefaan W. Van Gool *, Jennifer Makalowski, Peter Van de Vliet, Stefanie Van Gool, Tobias Sprenger, Volker Schirrmacher and Wilfried Stuecker

biomedicines

MDPI

Viewpoint

The Application of Evidence-Based Medicine in Individualized Medicine

Peter Van de Vliet *, Tobias Sprenger, Linde F. C. Kampers, Jennifer Makalowski, Volker Schirrmacher, Wilfried Stücker and Stefaan W. Van Gool

Check for updates

Editorial Commentary

Translational Cancer Research, 2023

Dendritic cell vaccination for glioblastoma multiforme patients: has a new milestone been reached?

Stefaan W. Van Gool^, Jennifer Makalowski, Linde F. C. Kampers, Peter Van de Vliet, Tobias Sprenger, Volker Schirrmacher, Wilfried Stücker

[Instruction: Revises AQ: Kindly note we have followed US spelling for this series. Hence, the correction "Towards" has not been followed in chapter title and retained the word "Toward" as is. Please check and confirm is this fine.]Methods

M1 behind oncolytic virus-based DC vaccines in cancer: Towards a multiphase combined treatment strategy for

Q4 Glioblastoma (GBM) patients

Q7Q8 Stefaan W. Van Gool*, vangool@iozk.de, Peter Van de Vliet, ~~Linde~~Linde F.C. Kampers, Jennifer ~~Makalowski~~Kosmal, Tobias Sprenger, Ella Reich, Volker Schirrmacher, Wilfried Stuecker

Q10Q9 ~~IOZK, Cologne, Germany~~Immun-onkologisches Zentrum Köln, Cologne, Germany

Methods in Cell Biology, in press

Treatment phase 3:
Maintenance and Expansion of Immune protection

Treatment phase 2:
Immunization

Treatment phase 1:
Anticancer treatment

Towards Control of GBM ?

Immunomodulatory strategies

Active specific immunotherapy with vaccines

Treatment-induced anticancer immunization
Direct anti-cancer activity

(Surgery)

Radiotherapy

Chemotherapy

Targeted therapy
Adoptive immunotherapy
Passive immunotherapy

Immunogenic cell death (ICD)
Immunotherapy
(Biologic / physics Therapy)

Tumor and host and their interaction are dynamic processes

Complementary medicines, Repurposed drugs
Real World Data have their own scientific and clinical value

Nobel Prize Medicine 2018

J. P. Allison, T. Honjo

Nobel Prize Medicine 2011

B. Beutler, J. Hoffmann, R. Steinman

Smart combination

Individualization

1. **Molecular biology**
2. **Tumor antigens**
3. **Tumor-host interaction**
4. **Immune system / inflammation**
5. **Treatment combination**
6. **Response to treatment**

Treatment adaptation

Treatment phase 1:
Anticancer treatment

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma

Roger Stupp, M.D., Warren P. Mason, M.D., Martin J. van den Bent, M.D., Michael Weller, M.D., Barbara Fisher, M.D., Martin J.B. Taphoorn, M.D., Karl Belanger, M.D., Alba A. Brandes, M.D., Christine Marosi, M.D., Ulrich Bogdahn, M.D., Jürgen Curschmann, M.D., Robert C. Janzer, M.D., Samuel K. Ludwin, M.D.,Thierry Gorlia, M.Sc., Anouk Allgeier, Ph.D., Denis Lacombe, M.D., J. Gregory Cairncross, M.D., Elizabeth Eisenhauer, M.D., and René O. Mirimanoff, M.D., for the European Organisation for Research and Treatment of Cancer Brain Tumor and Radiotherapy Groups and the National Cancer Institute of Canada Clinical Trials Group*

Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial

Lancet Oncol, 2009

Roger Stupp, Monika E Hegi, Warren P Mason, Martin J van den Bent, Martin J B Taphoorn, Robert C Janzer, Samuel K Ludwin, Anouk Allgeier, Barbara Fisher, Karl Belanger, Peter Hau, Alba A Brandes, Johanna Gijtenbeek, Christine Marosi, Charles J Vecht, Karima Mokhtari, Pieter Wesseling, Salvador Villa, Elizabeth Eisenhauer, Thierry Gorlia, Michael Weller, Denis Lacombe, J Gregory Cairncross, René-Olivier Mirimanoff; on behalf of the European Organisation for Research and Treatment of Cancer Brain Tumour and Radiation Oncology Groups and the National Cancer Institute of Canada Clinical Trials Group

Dose-Dense Temozolomide for Newly Diagnosed Glioblastoma: A Randomized Phase III Clinical Trial

Mark R. Gilbert, Meihua Wang, Kenneth D. Aldape, Roger Stupp, Monika E. Hegi, Kurt A. Jaeckle, Terri S. Armstrong, Jeffrey S. Wefel, Minhee Won, Deborah T. Blumenthal, Anita Mahajan, Christopher J. Schultz, Sara Erridge, Brigitta Baumert, Kristen I. Hopkins, Tzahala Tzuk-Shina, Paul D. Brown, Arnab Chakravarti, Walter J. Curran Jr, and Minesh P. Mehta **JCO, 2013**

A Randomized Trial of Bevacizumab for Newly Diagnosed Glioblastoma

Mark R. Gilbert, M.D., James J. Dignam, Ph.D., Terri S. Armstrong, Ph.D., A.N.P.-B.C., Jeffrey S. Wefel, Ph.D., Deborah T. Blumenthal, M.D., Michael A. Vogelbaum, M.D., Ph.D., Howard Colman, M.D., Ph.D., Arnab Chakravarti, M.D., Stephanie Pugh, Ph.D., Minhee Won, M.A., Robert Jeraj, Ph.D., Paul D. Brown, M.D., Kurt A. Jaeckle, M.D., David Schiff, M.D., Volker W. Stieber, M.D., David G. Brachman, M.D., Maria Werner-Wasik, M.D., Ivo W. Tremont-Lukats, M.D., Erik P. Sulman, M.D., Kenneth D. Aldape, M.D., Walter J. Curran, Jr., M.D., and Minesh P. Mehta, M.D. **NEJM, 2014**

Preliminary Communication

Maintenance Therapy With Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma
A Randomized Clinical Trial

JAMA, 2017

Roger Stupp, MD; Sophie Taillibert, MD; Andrew A. Kanner, MD; Santosh Kesari, MD, PhD; David M. Steinberg, PhD; Steven A. Toms, MD, FACS, MPH; Lynne P. Taylor, MD, FAAN; Frank Lieberman, MD; Antonio Silvani, MD; Karen L. Fink, MD, PhD; Gene H. Barnett, MD, MBA; Jay-Jiguang Zhu, MD, PhD; John W. Henson, MD, MBA, FAAN; Herbert H. Engelhard, MD, PhD; Thomas C. Chen, MD, PhD; David D. Tran, MD, PhD; Jan Sroubek, MD; Nam D. Tran, MD, PhD; Andreas F. Hottinger, MD, PhD; Joseph Landolfi, DO; Rajiv Desai, MD; Manuela Caroli, MD; Yvonne Kew, MD, PhD; Jerome Honnorat, MD, PhD; Ahmed Idbaih, MD, PhD; Eilon D. Kirson, MD, PhD; Uri Weinberg, MD, PhD; Yoram Palti, MD, PhD; Monika E. Hegi, PhD; Zvi Ram, MD

ECA

Rindopepimut with temozolomide for patients with newly diagnosed, EGFRvIII-expressing glioblastoma (ACT IV): a randomised, double-blind, international phase 3 trial

*Michael Weller, Nicholas Butowski, David D Tran, Lawrence D Recht, Michael Lim, Hal Hirte, Lynn Ashby, Laszlo Mechtler, Samuel A Goldlust, Fabio Iwamoto, Jan Drappatz, Donald M O'Rourke, Mark Wong, Mark G Hamilton, Gaetano Finocchiaro, James Perry, Wolfgang Wick, Jennifer Green, Yi He, Christopher D Turner, Michael J Yellin, Tibor Keler, Thomas A Davis, Roger Stupp, and John H Sampson, for the ACT IV trial investigators** **Lancet Oncol, 2017**

A Randomized Double-Blind Placebo-Controlled Phase II Trial of Dendritic Cell Vaccine ICT-107 in Newly Diagnosed Patients with Glioblastoma

Patrick Y. Wen[1], David A. Reardon[1], Terri S. Armstrong[2], Surasak Phuphanich[3], Robert D. Aiken[4], Joseph C. Landolfi[5], William T. Curry[6], Jay-Jiguang Zhu[7], Michael Glantz[8], David M. Peereboom[9], James M. Markert[10], Renato LaRocca[11], Donald M. O'Rourke[12], Karen Fink[13], Lyndon Kim[14], Michael Gruber[15], Glenn J. Lesser[16], Edward Pan[17], Santosh Kesari[18], Alona Muzikansky[19], Clemencia Pinilla[20], Radleigh G. Santos[20], and John S. Yu[21,22,23] **CCR, 2019**

JAMA Oncology | Original Investigation

Association of Autologous Tumor Lysate-Loaded Dendritic Cell Vaccination With Extension of Survival Among Patients With Newly Diagnosed and Recurrent Glioblastoma
A Phase 3 Prospective Externally Controlled Cohort Trial

JAMA Oncol, 2023

Phase III

Linda M. Liau, MD, PhD; Keyoumars Ashkan, MD, FRCP, FRCS; Steven Brem, MD; Jian L. Campian, MD, PhD; John E. Trusheim, MD; Fabio M. Iwamoto, MD; David D. Tran, MD, PhD; George Ansstas, MD; Charles S. Cobbs, MD; Jason A. Heth, MD; Michael E. Salacz, MD; Stacy D'Andre, MD; Robert D. Aiken, MD; Yaron A. Moshel, MD, PhD; Joo Y. Nam, MD; Clement P. Pillainayagam, MD; Stephanie A. Wagner, MD; Kevin A. Walter, MD; Rekha Chaudary, MD; Samuel A. Goldlust, MD; Ian Y. Lee, MD; Daniela A. Bota, MD, PhD; Heinrich Elinzano, MD; Jai Grewal, MD; Kevin Lillehei, MD; Tom Mikkelsen, MD, FRCPC; Tobias Walbert, MD; Steven Abram, MD; Andrew J. Brenner, MD, PhD; Matthew G. Ewend, MD; Simon Khagi, MD; Darren S. Lovick, MD; Jana Portnow, MD; Lyndon Kim, MD; William G. Loudon, MD; Nina L. Martinez, MD; Reid C. Thompson, MD; David E. Avigan, MD; Karen L. Fink, MD, PhD; Francois J. Geoffroy, MD; Pierre Giglio, MD; Oleg Gligich, MD; Dietmar Krex, MD; Scott M. Lindhorst, MD; Jose Lutzky, MD; Hans-Jörg Meisel, MD, PhD; Minou Nadji-Ohl, MD; Lhagva Sanchin, MD; Andrew Sloan, MD; Lynne P. Taylor, MD; Julian K. Wu, MD; Erin M. Dunbar, MD; Arnold B. Etame, MD, PhD; Santosh Kesari, MD, PhD; David Mathieu, MD; David E. Piccioni, MD, PhD; David S. Baskin, MD; Michel Lacroix, MD; Sven-Axel May, MD; Pamela Z. New, MD; Timothy J. Pluard, MD; Steven A. Toms, MD; Victor Tse, MD; Scott Peak, MD; John L. Villano, MD, PhD; James D. Battiste, MD, PhD; Paul J. Mulholland, MD; Michael L. Pearlman, MD; Kevin Petrecca, MD, PhD; Michael Schulder, MD; Robert M. Prins, PhD; Alton L. Boynton, PhD; Marnix L. Bosch, PhD

Treatment phase 1:
Anticancer treatment

frontiers in Oncology
REVIEW
published: 17 June 2015
doi: 10.3389/fonc.2015.00098

Brain tumor immunotherapy: what have we learned so far?

Stefaan Willy Van Gool *

ANTICANCER RESEARCH *39*: 2043-2051 (2019)
doi:10.21873/anticanres.13315

Immune Phenotype Correlates With Survival in Patients With GBM Treated With Standard Temozolomide-based Therapy and Immunotherapy

MARKOS ANTONOPOULOS[1], STEFAAN W. VAN GOOL[2], DIMITRA DIONYSIOU[1], NORBERT GRAF[3] and GEORGIOS STAMATAKOS[1]

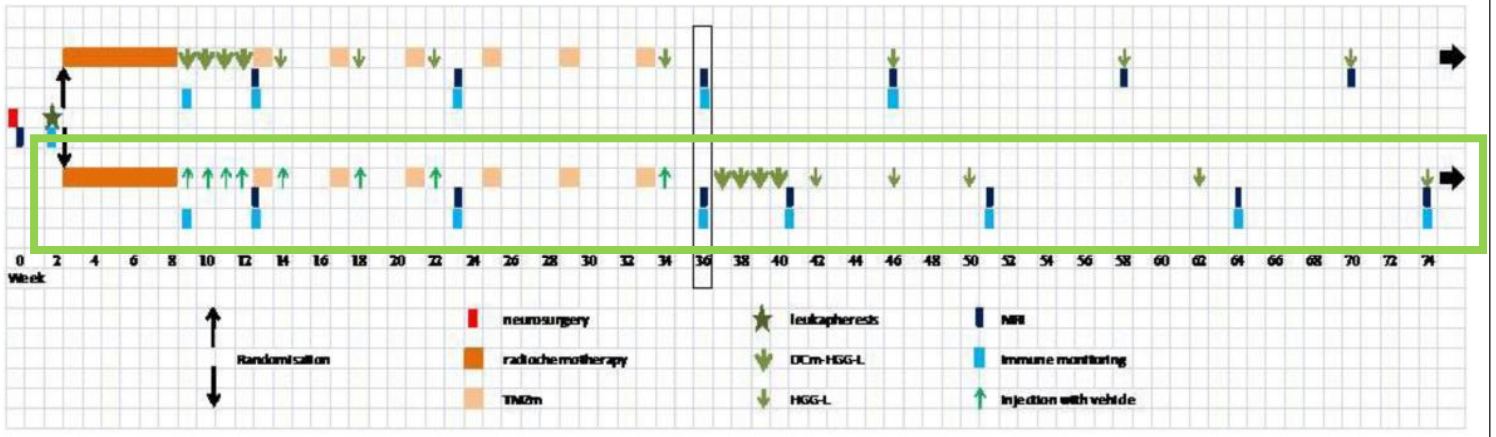


FIGURE 5 | Outline of the phase IIb randomized clinical trial HGG-2010.

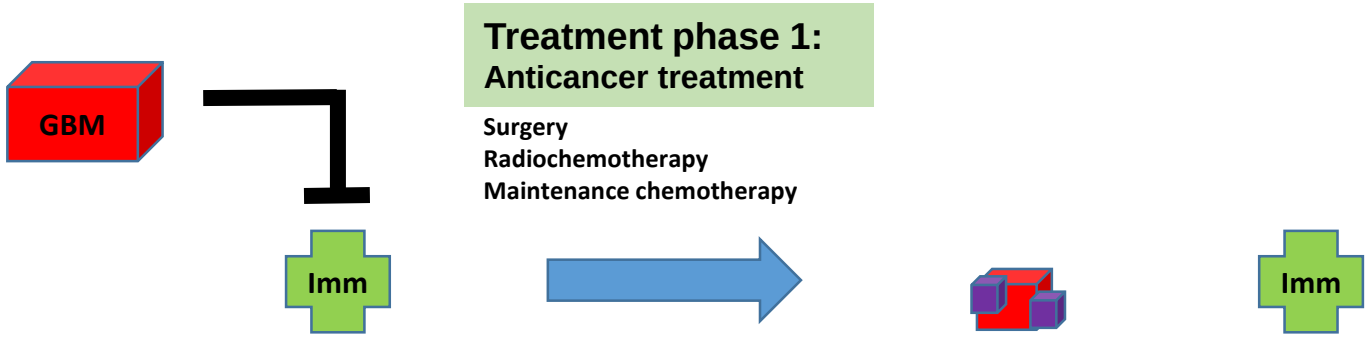
Table I. *Overall survival (OS) data of the total study population and subgroups residual tumor volume (RTV).*

Patient group	No. of patients	Median OS (months)	2-Year OS rate (%)	95%CI
Total group	101	19	33.66	24.66-42.88
Early vaccination, RTV=0	19	22	40.2	18.4-61.2
Late vaccination, RTV=0	29	23	44.8	26.5-61.5
Early vaccination, RTV>0	28	19	25	11-41.7
Late vaccination, RTV>0	25	16	28	12.4-46

240
Neuro-Oncology
23(2), 240–250, 2021 | doi:10.1093/neuonc/noaa247 | Advance Access date 1 November 2020

DNA methylation based glioblastoma subclassification is related to tumoral T-cell infiltration and patient survival

Joost Dejaegher*, Lien Solie, Zoé Hunin, Raf Sciot, David Capper, Christin Siewert, Sofie Van Cauter, Guido Wilms, Johan van Loon, Nadine Ectors, Steffen Fieuws, Stefan M. Pfister, Stefaan W. Van Gool, and Steven De Vleeschouwer



Cellular immunity of patients with malignant glioma: prerequisites for dendritic cell vaccination immunotherapy

J Neurosurg, 2006

Marion Rapp [1], Zakir Ozcan, Hans-Jakob Steiger, Peter Wernet, Michael C Sabel, Rüdiger V Sorg

Tumor Microenvironment and Immune Escape in the Time Course of Glioblastoma

Mol Neurobiol, 2022

Assunta Virtuoso[1,2] · Ciro De Luca[1] · Giovanni Cirillo[1] · Matteo Riva[3,4] · Gabriele Romano[5] · Angela Bentivegna[2] · Marialuisa Lavitrano[2] · Michele Papa[1,6] · Roberto Giovannoni[7]

Impact of Radiochemotherapy on Immune Cell Subtypes in High-Grade Glioma Patients

Front Oncol, 2020

Valérie Dutoit[1,2], Géraldine Philippin[1,2], Valérie Widmer[1,2], Eliana Marinari[1,2], Aurélie Vuilleumier[3], Denis Migliorini[1,2], Karl Schaller[4] and Pierre-Yves Dietrich[1,2,3]*

Malignant Gliomas as Second Neoplasms in Pediatric Cancer Survivors: Neuropathological Study

BioMed Res Int, 2018

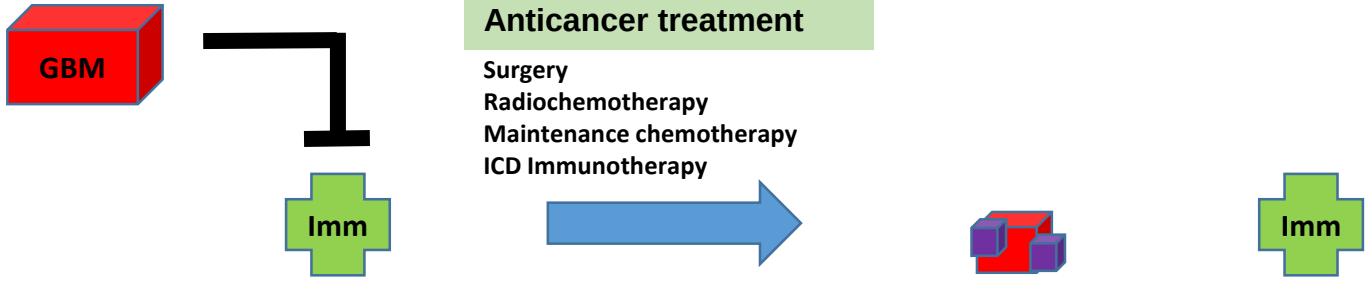
Ewa Izycka-Swieszewska,[1] Ewa Bien,[2] Joanna Stefanowicz,[2] Edyta Szurowska,[3] Ewa Szutowicz-Zielinska,[4] Magdalena Koczkowska,[5] Dawid Sigorski,[6] Wojciech Kloc,[7,8] Wojciech Rogowski,[9] and Elzbieta Adamkiewicz-Drozynska[2]

Neuro-Oncology Advances
4(1), 1–14, 2022 | https://doi.org/10.1093/noajnl/vdac076 | Advance Access date 23 May 2022

Neuro-Oncol Adv, 2022

Detection of temozolomide-induced hypermutation and response to PD-1 checkpoint inhibitor in recurrent glioblastoma

Paul Daniel, Brian Meehan, Siham Sabri, Fatemeh Jamali, Jann N. Sarkaria, Dongsic Choi, Delphine Garnier, Gaspar Kitange, Kate I. Glennon, Antoine Paccard, Jason Karamchandani, Yasser Riazalhosseini, Janusz Rak†, and Bassam Abdulkarim†



Treatment phase 1:
Anticancer treatment

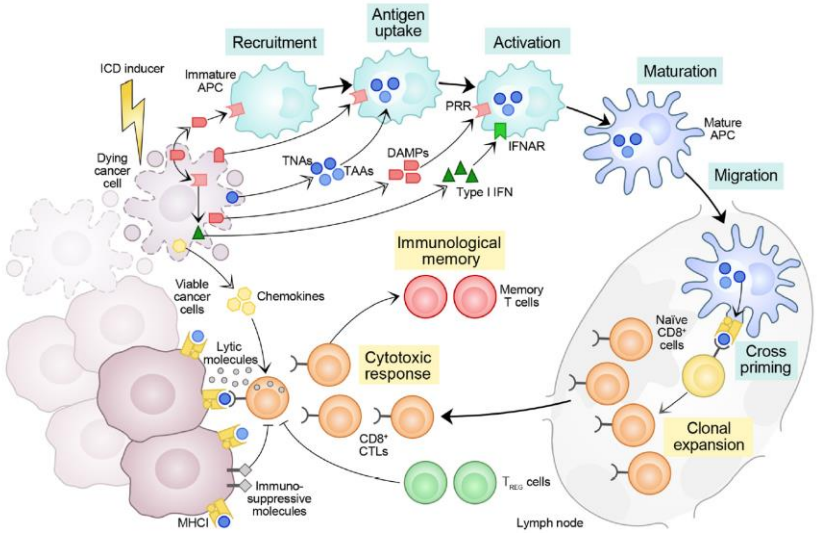
Surgery
Radiochemotherapy
Maintenance chemotherapy
ICD Immunotherapy

Journal for ImmunoTherapy of Cancer

JITC, 2020

Consensus guidelines for the definition, detection and interpretation of immunogenic cell death

Lorenzo Galluzzi,[1,2,3,4,5] Ilio Vitale,[6,7] Sarah Warren,[8] Sandy Adjemian,[9,10] Patrizia Agostinis,[11,12] Aitziber Buqué Martinez,[1] Timothy A Chan,[13,14] George Coukos,[15] Sandra Demaria,[1,2,16] Eric Deutsch,[17,18,19] Dobrin Draganov,[20] Richard L Edelson,[4,21] Silvia C Formenti,[1,2] Jitka Fucikova,[22,23] Lucia Gabriele,[24] Udo S Gaipl,[25] Sofia R Gameiro,[26] Abhishek D Garg,[11] Encouse Golden,[1,2] Jian Han,[27] Kevin J Harrington,[28,29] Akseli Hemminki,[30,31] James W Hodge,[26] Dewan Md Sakib Hossain,[32] Tim Illidge,[33] Michael Karin,[34] Howard L Kaufman,[35,36] Oliver Kepp,[37,38] Guido Kroemer,[5,37,38,39,40,41,42,43,44] Juan Jose Lasarte,[45] Sherene Loi,[46,47] Michael T Lotze,[48,49,50] Gwenola Manic,[6,7] Taha Merghoub,[51,52,53] Alan A Melcher,[54] Karen L Mossman,[55] Felipe Prosper,[56] Øystein Rekdal,[57,58] Maria Rescigno,[59,60] Chiara Riganti,[61,62] Antonella Sistigu,[63,64] Mark J Smyth,[65] Radek Spisek,[22,23] John Stagg,[66,67,68] Bryan E Strauss,[69] Daolin Tang,[70] Kazuki Tatsuno,[4] Stefaan W van Gool,[71] Peter Vandenabeele,[9,10,72] Takahiro Yamazaki,[1] Dmitriy Zamarin,[73,74] Laurence Zitvogel,[39,75,76,77,78] Alessandra Cesano,[79] Francesco M Marincola[80]



J Neurooncol (2010) 98:395–405
DOI 10.1007/s11060-009-0093-0

CLINICAL STUDY - PATIENT STUDY

Transcranial electro-hyperthermia combined with alkylating chemotherapy in patients with relapsed high-grade gliomas: phase I clinical results

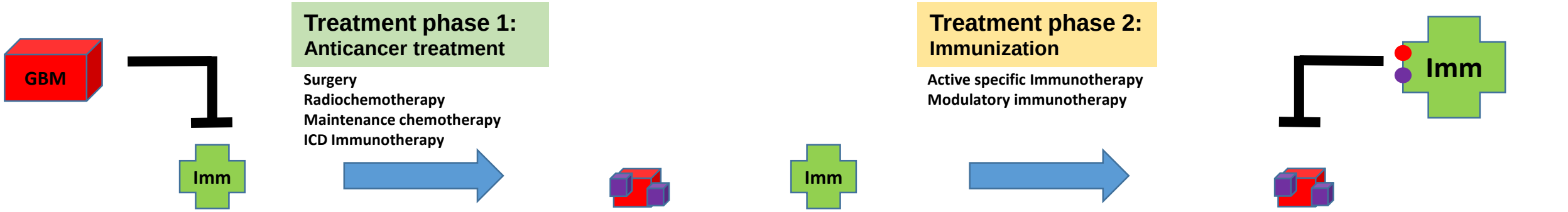
Caecilia Wismeth · Christine Dudel · Christina Pascher · Paul Ramm · Torsten Pietsch · Birgit Hirschmann · Christiane Reinert · Martin Proescholdt · Petra Rümmele · Gerhard Schuierer · Ulrich Bogdahn · Peter Hau

OPEN

Newcastle disease virus enhances the growth-inhibiting and proapoptotic effects of temozolomide on glioblastoma cells in vitro and in vivo

Received: 7 November 2017
Accepted: 9 July 2018
Published online: 31 July 2018

Yang Bai[1], Yong Chen[1], Xinyu Hong[1], Xinrui Liu[1], Xing Su[2], Shanji Li[1], Xuechao Dong[1], Gang Zhao[1] & Yunqian Li[1]



1

OPEN ACCESS Freely available online — PLOS | ONE

Clinical Efficacy of Tumor Antigen-Pulsed DC Treatment for High-Grade Glioma Patients: Evidence from a Meta-Analysis

PLOS-One, 2014

Jun-Xia Cao[1,2]*, Xiao-Yan Zhang[1], Jin-Long Liu[1], Duo Li[1], Jun-Li Li[1], Yi-Shan Liu[1], Min Wang[1], Bei-Lei Xu[1], Hai-Bo Wang[1], Zheng-Xu Wang[1]*

2

Dendritic Cell-Based Vaccine for the Treatment of Malignant Glioma: A Systematic Review

Xuan Wang, Hong-Yang Zhao, Fang-Cheng Zhang, Yun Sun, Zhi-Yong Xiong & Xiao-Bing Jiang

Cancer Invest, 2014

3

Therapeutics and Clinical Risk Management — Dovepress, open access to scientific and medical research

Open Access Full Text Article — REVIEW

Dendritic cell vaccines for high-grade gliomas

Eagles ME, et al, 2018

This article was published in the following Dove Press journal: Therapeutics and Clinical Risk Management

4

Assessment of efficacy of dendritic cell therapy and viral therapy in high grade glioma clinical trials. A meta-analytic review

JII, 2019

Bogdan Ionel Vatu, Stefan-Alexandru Artene, Adeline-Georgiana Staicu, Adina Turcu-Stiolica, Catalin Folcuti, Alexandra Dragoi, Catalina Cioc, Stefania-Carina Baloi, Ligia Gabriela Tataranu, Cristian Silosi & Anica Dricu

5

CLINICAL CANCER RESEARCH | PERSPECTIVES

Once, Twice, Three Times a Finding: Reproducibility of Dendritic Cell Vaccine Trials Targeting Cytomegalovirus in Glioblastoma

CCR, 2020

Kristen A. Batich[1,2,3], Duane A. Mitchell[4,5], Patrick Healy[1,6], James E. Herndon II[1,6], and John H. Sampson[1,3]

6

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Contents lists available at ScienceDirect

International Immunopharmacology

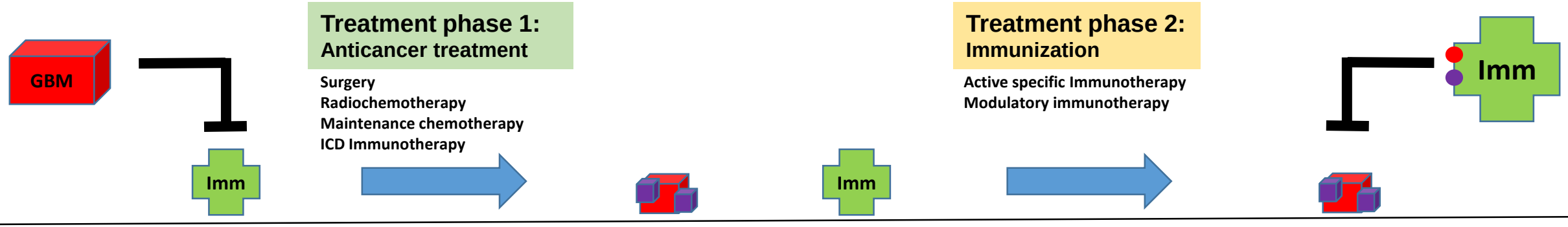
journal homepage: www.elsevier.com/locate/intimp

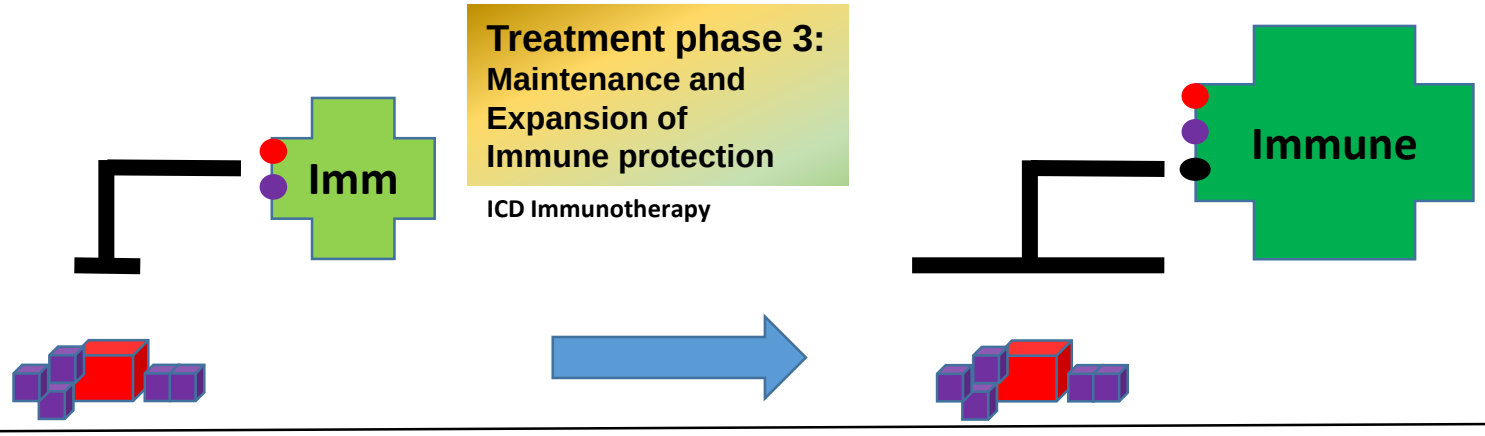
Efficacy and safety of dendritic cell vaccines for patients with glioblastoma: A meta-analysis of randomized controlled trials

IIP, 2020

Li Lv[1], Jiangchao Huang[1], Haipeng Xi, Xiangyang Zhou*

Department of Neurosurgery, First Affiliated Hospital, University of South China, Hengyang 421001, Hunan Providence, China





Modulatory immunotherapy

- Anti-inflammation: anti-HR1, Cox2 inhibitor, Curamun
- CPI if needed
- Risedronate

Neuron-Glioma axis

Metabolic cocktail

- Metformin
- Atorvastatin
- Mebendazol

Neuro-psycho-endocrino-immunology axis

Melatonin

Modulated Electrohyperthermia in Integrative Cancer Treatment for Relapsed Malignant Glioblastoma and Astrocytoma: Retrospective Multicenter Controlled Study

Integrative Cancer Therapies
1–11

DOI: 10.1177/1534735418812691
journals.sagepub.com/home/ict
SAGE

Integrative Cancer Therapy, 2018

Giammaria Fiorentini, MD[1], Donatella Sarti, PhD[1], Carlo Milandri, MD[2], Patrizia Dentico, MD[2], Andrea Mambrini, MD[3], Caterina Fiorentini, MD[4], Gianmaria Mattioli, MD[1], Virginia Casadei, MD[1] and Stefano Guadagni, MD[5]

Phase I/II Trial of Intravenous NDV-HUJ Oncolytic Virus in Recurrent Glioblastoma Multiforme

Molecular Therapy, 2006

Arnold I. Freeman,[1] Zichria Zakay-Rones,[2] John M. Gomori,[3] Eduard Linetsky,[4,5] Linda Rasooly,[1] Evgeniya Greenbaum,[2] Shira Rozenman-Yair,[6] Amos Panet,[2] Eugene Libson,[7] Charles S. Irving,[6] Eithan Galun,[1,*] and Tali Siegal[5]

Dendritic cell–based immunotherapy targeting Wilms' tumor 1 in patients with recurrent malignant glioma

J Neurosurg, 2015

Keiichi Sakai, MD, PhD,[1,11] Shigetaka Shimodaira, MD, PhD,[2] Shinya Maejima, MD, PhD,[3] Nobuyuki Udagawa, DDS, PhD,[3] Kenji Sano, MD, PhD,[4] Yumiko Higuchi, PhD,[2] Terutsugu Koya, MS,[2] Takanaga Ochiai, DDS, PhD,[5] Masanori Koide, DDS, PhD,[6] Shunsuke Uehara, PhD,[7] Midori Nakamura, DDS, PhD,[7] Haruo Sugiyama, MD, PhD,[8] Yoshikazu Yonemitsu, MD, PhD,[9] Masato Okamoto, DDS, PhD,[10] and Kazuhiro Hongo, MD, PhD[1]

Phase IIa Study of SurVaxM Plus Adjuvant Temozolomide for Newly Diagnosed Glioblastoma

JCO, 2023

Manmeet S. Ahluwalia, MD[1]; David A. Reardon, MD[2]; Ajay P. Abad, MD[3]; William T. Curry, MD[4]; Eric T. Wong, MD[5]; Sheila A. Figel, PhD[6,7]; Laszlo L. Mechtler, MD[3]; David M. Peereboom, MD[1]; Alan D. Hutson, PhD[8]; Henry G. Withers, PhD[8]; Song Liu, PhD[8]; Ahmed N. Belal, MD[9]; Jingxin Qiu, MD, PhD[10]; Kathleen M. Mogensen, NP[3]; Sanam S. Dharma, PhD[6]; Andrew Dhawan, MD[11]; Meaghan T. Birkemeier, BS[6]; Danielle M. Casucci, BS[6,7]; Michael J. Ciesielski, PhD[6,7]; and Robert A. Fenstermaker, MD[6,7]

cancers

MDPI

Article

Individualized Multimodal Immunotherapy for Adults with IDH1 Wild-Type GBM: A Single Institute Experience

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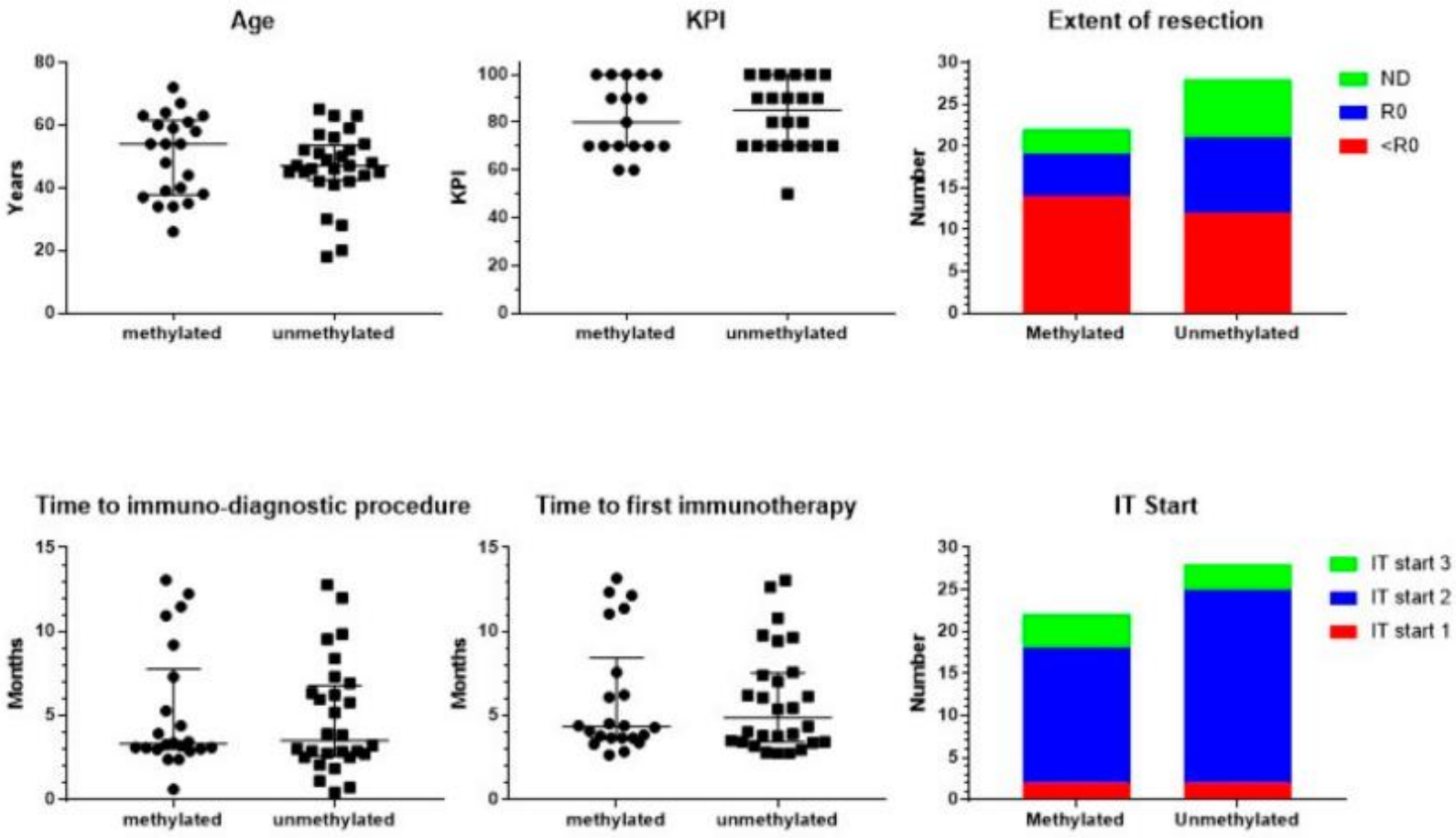
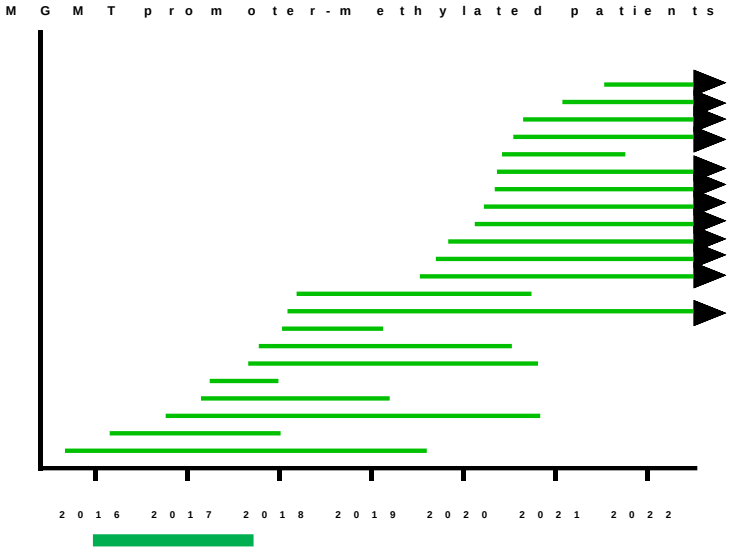
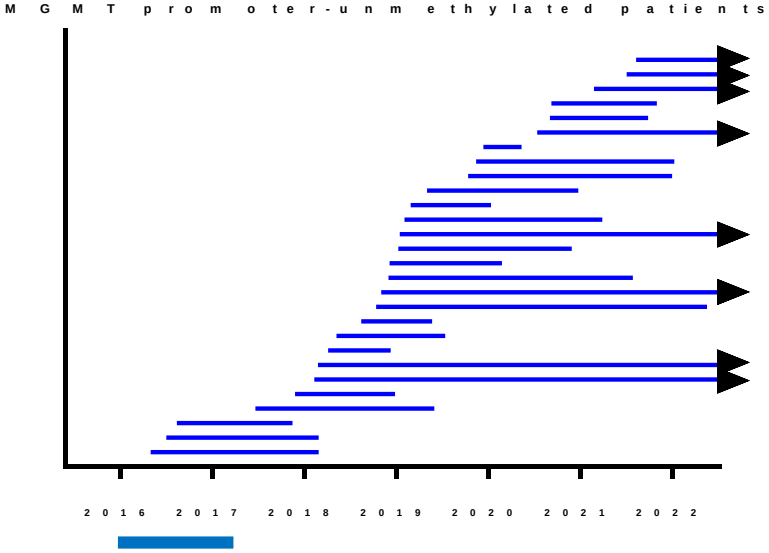
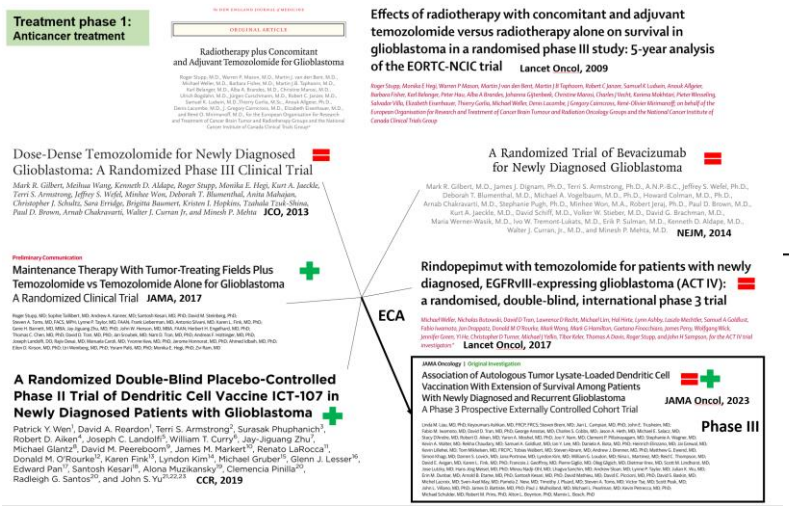








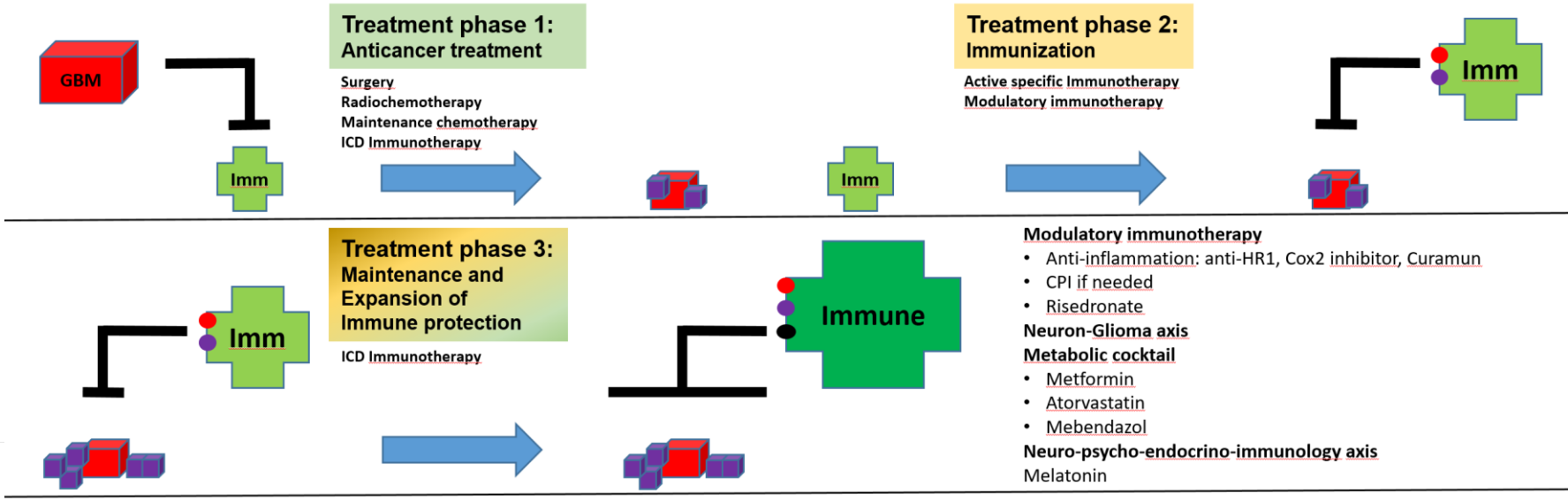
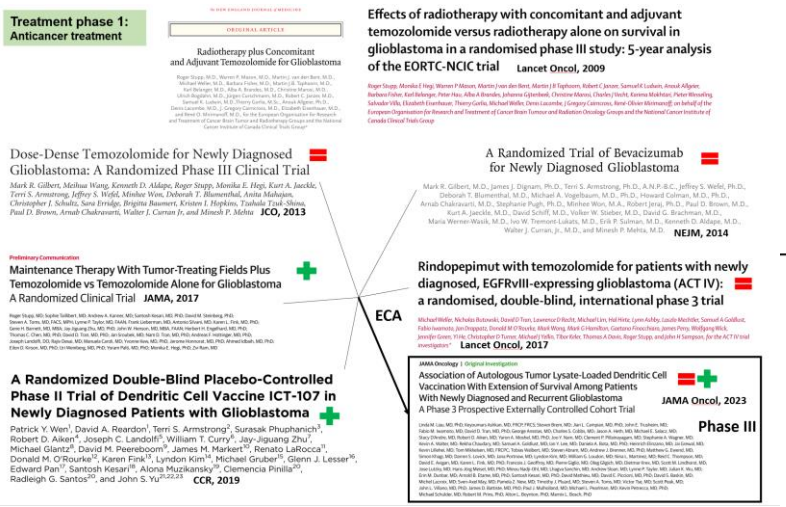


Table 3: Patient characteristics in the selected publications

	n	Median age	F/M (%)	Median KPI	Meth (%)	Unmeth (%)	R0 (%)	<R0 (%)	ND (%)
Gilbert [283]	411	>50	42/58	>90	30	62	46	44	0
Gilbert [284]	309	>50	37/63	>90	28	69	59	41	0
Stupp [228]	229	57	31/69	90	42	51	54	46	0
Weller [285]	374	58	39/61	>70	35	58	56	44	0
Wen [81]	43	60	28/72	>90	42	56	74	26	0
Liau [10, 11]	232	56	41/59	>90	39	56	63	37	0
Van Gool [106]	50	48	46/54	80	44	56	28	52	20

F: female; M: male; KPI: Karnofsky performance index; Meth: MGMT promoter-methylated; Unmeth: MGMT promoter-unmethylated; ND: not documented; R0: complete resection; <R0: less than complete resection

[Instruction: Revises AQ: Kindly note we have followed US spelling for this series. Hence, the correction "Towards" has not been followed in chapter title and retained the word "Toward" as is. Please check and confirm is this fine.]Methods behind oncolytic virus-based DC vaccines in cancer: Towards a multiphase combined treatment strategy for Glioblastoma (GBM) patients



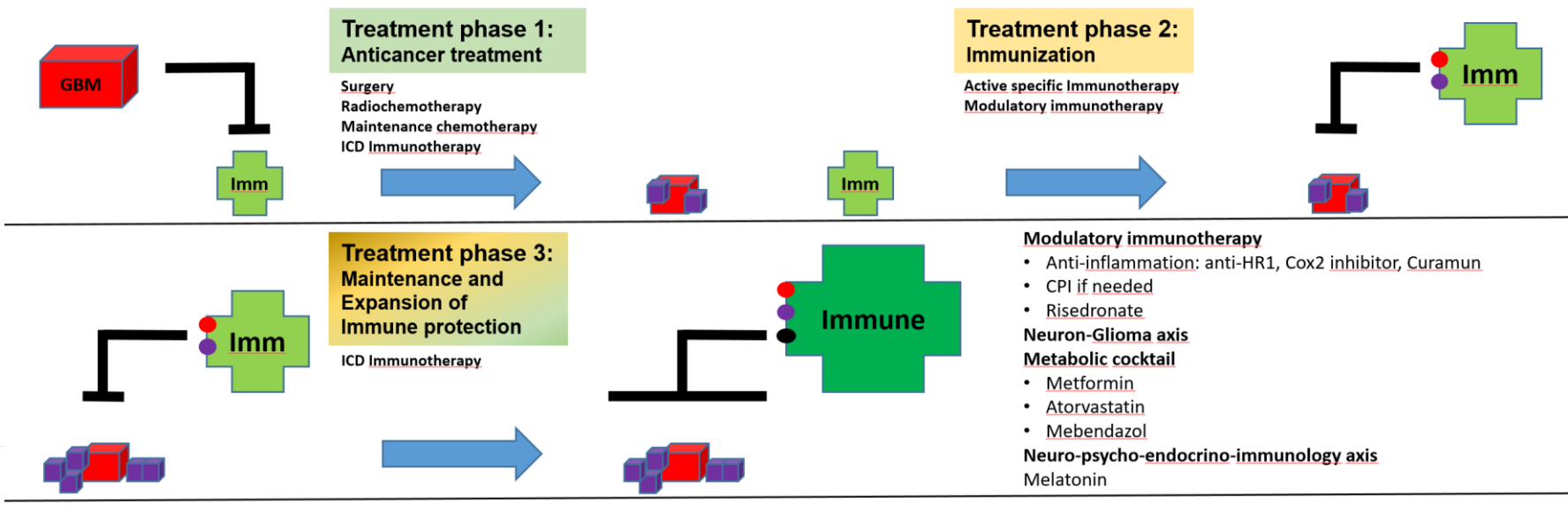


Table 4: Overall survival reported in selected publications

Reference		Unmethylated mOS (m)	Unmethylated 2y OS (%)	Methylated mOS (m)	Methylated 2y OS (%)
Stupp [195] RCT	S + RT	11,8	1,8	15,3	23,9
	S + RCT + CT	12,6	14,8	23,4	48.9
Stupp [228] RCT	**S + RCT + CT**	**14,7**	**22,1**	**21,2**	**37,7**
	S + RCT + CT + TTF	16,9	26,8	31,6	59,1
Liau [11] ECA	**S + RCT + CT**	**14,6**	**21**	**21,3**	**42**
	S + RCT + CT + DCVax®-L	14,9	19	30,2	58
Van Gool [106] RWD	S + RCT + CT + IMI	22,1	41,6	37,7	80,5

IMI: individualized multimodal immunotherapy; m: months; mOS: median overall survival RCT: randomized controlled trial; RDW: real-world data; S + RT: surgery + radiotherapy; S + RCT + CT: surgery + radiochemotherapy + chemotherapy; TTF: tumor-treating fields; 2y OS: two-year overall survival. Expected OS with standard of care treatment anno 2023 are marked in bold and gray background.

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Treatment phase 3:
Maintenance and Expansion of Immune protection

Treatment phase 2:
Immunization

Treatment phase 1:
Anticancer treatment

Towards Control of GBM ?

Immunomodulatory strategies

Active specific immunotherapy with vaccines

Treatment-induced anticancer immunization
Direct anti-cancer activity

- (Surgery)
- Radiotherapy
- Chemotherapy
- Targeted therapy
  Adoptive immunotherapy
  Passive immunotherapy
- Immunogenic cell death (ICD)
  Immunotherapy
  (Biologic / physics Therapy)

Tumor and host and their interaction are dynamic processes

Complementary medicines, Repurposed drugs
Real World Data have their own scientific and clinical value

Nobel Prize Medicine 2018

J. P. Allison, T. Honjo

Nobel Prize Medicine 2011

B. Beutler, J. Hoffmann, R. Steinman

Smart combination

Individualization

1. Molecular biology
2. Tumor antigens
3. Tumor-host interaction
4. Immune system / inflammation
5. Treatment combination
6. Response to treatment

Treatment adaptation

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