

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med* 2005;353:1659-72.

## Supplementary Appendix 1 Approved chemotherapy regimens for the HERA Trial

Regimen class	Regimens
ALL REGIMENS	Patient must have received at least four cycles of an approved (neo-) adjuvant chemotherapy regimen. In all cases, the maximum cumulative allowable dose of doxorubicin (A) is 360mg/m <sup>2</sup> and of epirubicin (E) is 720mg/m <sup>2</sup>
Anthracyclines with no taxanes	<p>Regimens in this category that are allowed for the HERA trial include the association of either A or E with cyclophosphamide (C) with or without 5-fluorouracil (F), and A or E as single agents or combined with C and followed by several cycles of CMF (where M is methotrexate).</p> <p><u>Minimum allowable starting doses of A or E associated with C with or without F:</u></p> <p>AC: 60mg/m<sup>2</sup>  CAF/FAC: 50mg/m<sup>2</sup> (q21d or q28d)  EC: 90mg/m<sup>2</sup>  75mg/m<sup>2</sup> (day 1 q21d) if given for a minimum of 6 cycles  FEC/CEF: 50mg/m<sup>2</sup> (days 1 and 8 q28d)  75mg/m<sup>2</sup> (day 1 q21d)  60mg/m<sup>2</sup> (day 1 q21d) if given for a minimum of 5 cycles</p> <p><u>Minimum allowable starting doses of A or E as single agents or combined with C and followed by CMF (described below):</u></p> <p>A: 75mg/m<sup>2</sup>  E: 90mg/m<sup>2</sup></p>
Anthracyclines and taxanes	<p>Regimens in this category that are allowed for the HERA trial include sequential or combined anthracyclines (A or E) and taxanes (paclitaxel [P] and docetaxel [D]). A or E may be combined with C with or without F.</p> <p><u>Minimum allowable starting doses of A or E (with or without C and/or F) followed by P or D (sequential regimens):</u></p> <p>A: 60mg/m<sup>2</sup>  FAC: 50mg/m<sup>2</sup>  E: 90mg/m<sup>2</sup>  60mg/m<sup>2</sup> (day 1 q21d) if followed by D 100mg/m<sup>2</sup> (day 1 q21d) if given for a minimum of 5 cycles  FEC: 75mg/m<sup>2</sup>  P: 175mg/m<sup>2</sup>/3-hour  75 mg/m<sup>2</sup> (q7d)  D: 100mg/m<sup>2</sup></p> <p><u>Minimum allowable starting doses of A and E (with or without C and/or F), and P and D given concurrently (combined regimens):</u></p> <p>A: 50mg/m<sup>2</sup>  E: 75mg/m<sup>2</sup>  P: 135mg/m<sup>2</sup>/3-hour  D: 60mg/m<sup>2</sup>/1-hour</p>
Non-anthracycline regimens	<p>Regimens in this category that are allowed for the HERA trial include C combined with methotrexate (M) and F (CMF). The minimum starting dose of C is 100mg/m<sup>2</sup>/day days 1-14 if given orally and 600mg/m<sup>2</sup> per injection if given intravenously. The recommended starting dose per injection of M is 40mg/m<sup>2</sup> and of F is 600mg/m<sup>2</sup>.</p> <p>CMF given day 1 and 8 every 28 days with oral C is the preferred schedule. Other CMF schedules are acceptable but should be used preferentially in patients who cannot tolerate oral C.</p>
Other regimens	Any regimen that is part of a chemotherapy trial which has been approved a priori by the HERA Executive Committee <sup>A</sup>

<sup>A</sup> An updated list of these trials can be obtained from the BrEAST Data Centre. Chemotherapy trials that are initiated while recruitment to the HERA trial is ongoing can be added to this list following approval from the Executive Committee.

Legend: A=doxorubicin; C=cyclophosphamide; D=docetaxel; E=epirubicin; F=5-fluorouracil; M=methotrexate; P=paclitaxel; T=taxane

## Supplementary Appendix 2 – Additional Acknowledgements

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The following clinicians entered patients in the trial:

M Lichinitser, N.N. Blokhin Cancer Research Center, Moscow (105); I Lang, National Institute of Oncology, Budapest (94); H Iwata, Aichi Cancer Center, Aichi (53); U Nitz, Universitaetsklinikum, Duesseldorf (53); V Müller, Universitaetsklinik Eppendorf, Hamburg (53); G Steger, Akh Univ. Kliniken Wien, Wien (51); A Wardley, Christie Hospital, Manchester (47); I Smith, Royal Marsden Hospital and Institute of Cancer Research, London (44); J Baselga, Vall d'Hebron University Hospital, Barcelona (44); Ri Lopez Sanchez, Isthmian Medical Research Center, Panama (43); N Harbeck, Krankenhaus Rechts Der Isar, Muenchen (43); L Gianni, Istituto Nazionale Per Lo Studie E La Cura Dei Tumori, Milano (43); R Khasanov, Tatarstan Republic Oncological Hospital, Kazan (41); C Barrios, Hospital Sao Lucas Da PUCRS, Porto Alegre (41); P Mallmann, Universitaet Koeln, Koeln (39); P Lohrmann, Klinikum Lippe Lemgo, Lemgo (39); F Feng-Yi, Chinese Academy Of Medical Science, Cancer Institute & Hospital, Beijing (39); C Huang, National Taiwan University Hospital, Taipei (36); V Semiglazov, Petrov Research Institute Of Oncology, St. Petersburg (36); M Piccart, Jules Bordet Institute, Brussels (35); M Untch, Universtaetsklinikum Grosshadern, Muenchen (35); E Vrdoljak, University Hospital Split, Split (34); L Tseng, Veterans General Hospital, Taipei (33); J Mayordomo, Hosp. Clinico Universitario De Zaragoza, Zaragoza (33); S Yu, Tongji Medical University, Wuhan (32); I Ron, Ichiluv Medical Centre, Tel Aviv (32); M Eckart, Onkologische Schwerpunktpraxis, Erlangen (31); Z Shen, Cancer Hospital, Fudan University, Shanghai (30); A Lluch Hernandez, Hospital Clinico Universitario De Valencia, Valencia (28); C Koehne, Staedt. Kliniken Gmbh, Oldenburg (28); J Jassem, Medical University, Gdansk (28); C Price, Bristol Oncology Centre, Bristol (27); A Vindevoghel,

Sainte-Elisabeth Hospital, Namur (27); E Jakobsen, Vejle Sygehus, Vejle (26); J Pedrini, Hospital Nossa Senhora Da Conceição, Ameh, Porto Alegre (26); A Goldhirsch, Instituto Europeo Di Oncologia, Milano (25); A Pluzanska, Medical Academy Of Lodz, Lodz (25); C Mendiola, Hospital Universitario 12 De Octubre, Madrid (25); M Toi, Tokyo Metropolitan Komagome General Hospital, Tokyo (25); A Veronesi, Centro Di Riferimento Oncologico, Aviano (25); K I Pritchard, Toronto Sunnybrook Regional Cancer Centre, Toronto (24); J Bergh, Karolinska Hospital, Stockholm (24); M Climent, Instituto Valenciano De Oncologia, Valencia (24); D Otero-Reyes, Hospital Cima San Jose, San Jose De Costa Rica (23); M Hall, Mount Vernon Hospital, Middlesex (23); M Brunt, University Hospital Of North Staffordshire, Staffordshire Oncology Centre, Stoke-On-Trent (23); P Sanchez-Rovira, Hospital General De Especialidades Ciudad De Jaen, Jaen (22); S Song, The Pla 307 Hospital, Beijing (22); C Focan, Clinique St-Joseph, Liege (22); S-Chen, Chang-Gung Memorial Hospital - (Lin Kou), Taoyuan (22); F Haslbauer, Lkh Voecklabruck, Voecklabruck (21); J Degreve, Az Vub, Medische Oncologie, Brussels (21); Z Guan, Sun Yat-Sen University Of Medical Science, Cancer Center, Guangzhou (21); R Agrawal, Royal Shrewsbury Hospitals NHS Trust, Shrewsbury (21); C Lohrisch, British Columbia Cancer Agency, Vancouver Centre, Vancouver (21); R Greil, Lkh Salzburg, Salzburg (21); G Perez-Manga, Hospital Gregorio Maranon, Madrid (21); N Bengtsson, University Hospital 5, Umea (21); Y Bang, Seoul National University Hospital, Seoul (21); R Coombes, Charing Cross Hospital, London (20); P Gascon, Hospital Clinic I Provincial, Barcelona (20); D Wallwiener, Universitaetsklinikum, Tuebingen (20); T Chao, Tri-Service General Hospital, Taipei (19); B Kaufman, Sheba Tel Hashomer, Ramat Gan (19); S Chen, Changhua Christian Hospital, Changhua (19); T Suarez Sahui, Hospital Regional Issste Merida, Merida (19); C Sohn, Universtaetskliniken, Heidelberg (19); R Kadlec, F.D. Roosevelt Hospital, Banska Bystrica (18); F Morales-Vasques, Instituto Nacional De Cancerologia, Mexico City (18); D Dodwell, Cookridge Hospital, Leeds (18); D Cameron, Western General Hospital, Edinburgh (18); B Thurlimann, Kantonsspital St. Gallen, St. Gallen (18); V Haahr, Viborg-Kjellerup Sygehus, Viborg (18); E Wist, Ulleval Sykehus, Oslo (17); M Clemens, Mutterhaus Der Borromaeerinnen, Trier (17); H Stehle, Marienhospital, Stuttgart (17); T Pienkowski, Instytut Onkologii,

Warszawa (17); J Baltzer, Klinikum Krefeld, Krefeld (17); T Delozier, Centre Francois Baclesse, Caen (17); Y Im, Sungkyunkwan University, School Of Medicine, Samsung Medical Centre, Seoul (17); J Passos Coelho, Ipo Francisco Gentil - Lisboa, Lisboa (17); M Cvetanovic, Marienhospital, Herne (17); A Von Der Assen, Franziskushospital, Georgsmarienhuetten (17); S Jiao, General Hospital Of P.L.A, Beijing (17); B Utracka-Hutka, Oncologic Center, Gliwice (17); C Hamm, Windsor Regional Cancer Centre, Windsor (17); B Nordenskjold, University Hospital 58/85, Linkoping (17); K Aogi, National Shikoku Cancer Center, Ehime (17); A Sami, Saskatoon Cancer Centre, University Of Saskatoon Campus, Saskatoon (17); V Srimuninnimit, Faculty Of Medicine Siriraj Hospital, Bangkok (16); J Hackmann, Marien-Hospital Witten, Witten (16); M Szucs, Hospital Of Bacs-Kiskun County, Kecskemet (16); Hm Enzinger, Westpfalz-Klinikum Kaiserslautern, Kaiserslautern (16); S O'Reilly, Clatterbridge Center For Oncology, Merseyside (16); J Schornagel, Antoni Van Leeuwenhoek Ziekenhuis, Amsterdam (16); C Boni, Arcispedale Santa Maria Nuova, Reggio Emilia (16); J Nortier, Leids Universitair Medisch Centrum, Leiden (15); K Roznowski, Medical University, Poznan (15); C Kamby, Kas Herlev, Herlev (15); E Forsthuber, Lkh Klagenfurt, Klagenfurt (15); K White, St. John Of God Hospital, Geelong (15); G Jerusalem, Chu Sart Tilman, Liege (15); M Benavides, Hospital Carlos Haya, Malaga (15); D Ritchie, Beatson Oncology Centre, Glasgow (15); M Borms, Cazk Groeninghe - Campus Maria's Voorzienigheid, Oncologisch Centrum, Kortrijk (14); S Schuhnecht, Nordstadt-Krankenhaus, Hannover (14); M Beckmann, University Hospital Erlangen, Erlangen (14); Á Mayer, Municipal Hospital Of Uzsoki Utca, Budapest (14); T Steck, Klinikum Chemnitz Gmbh, Chemnitz (14); W Lichtenegger, Charite-Berlin, Berlin (14); D Vorobiof, Sandton Oncology Centre, Johannesburg (14); Y Tokuda, Tokai University School Of Medicine, Kanagawa (14); M Andersson, Rigshospitalet, Koebenhavn (14); A Branson, Newcastle General Hospital, Newcastle-Upon-Tyne (13); H Minami, National Cancer Center Hospital East, Chiba (13); I Koza, National Cancer Institute, Bratislava (13); T Schwenzer, Staedt. Kliniken Dortmund, Dortmund (13); N Voravud, Chulalongkorn Hospital, Bangkok (13); T Noesselt, Kreiskrankenhaus Hameln, Hameln (13); H Samonigg, Lkh Graz, Graz (13); R Bell, Geelong Hospital, Andrew Love Cancer Centre, Geelong (13); V Harvey, Auckland Hospital, Auckland

(13); M Baki, Szent Margit Hospital, Budapest (13); E Galligioni, Centro Ospedaliero Santa Chiara, Trento (13); M Ramos Vazquez, Centro Oncologico De Galicia Jose Antonio Quiroga Y Pineyro, La Coruna (13); L Zetina Toache, Hospital Roosevelt, Guatemala (13); L Cirera, Hospital Mutua De Terrasa, Terrasa-Barcelona (13); G Emons, Universitaetsklinik, Goettingen (13); F Artioli, Ospedale " Ramazzini ", Carpi (12); E Young, Royal Preston Hospital, Preston (12); J McAleer, Belfast City Hospital, Belfast (12); A Coumbos, Universitaetsklinikum Benjamin Franklin, Berlin (12); S Cold, Odense University Hospital, Odense (12); L Kiesel, Universitaetsklinikum, Muenster (12); M Grgic, University Hospital Rebrow, Zagreb (12); A Lazarev, Altay Oncological Center, Barnaul (12); T Yang, Mackay Memorial Hospital, Taipei (12); J Bines, Instituto Nacional Do Cancer, Rio De Janeiro (12); M Bari, Presidi Ospedalieri Di Noale, Noale (12); A Gatzweiler, Univsersitaetsklinikum Dresden, Dresden (12); P Grundtvig Sorensen, Roskilde Amtssygehuset, Roskilde (12); G Pinotti, Ospedale Di Circolo, Fondazione Macchi, Varese (12); P Hupperets, Univers. Hosp. Maastricht, Maastricht (12); M Hou, Kaohsiung Medical University Chung-Ho Hospital, Kaohsiung (12); T Hickish, Royal Bournemouth Hospital, Bournemouth (11); A Farris, Universita- Istituto Clinica Medica, Sassari (11); K Khoo, National Cancer Centre, Singapore (11); L Iglesias Perez, Hospital Universitario Virgen Del Rocio, Sevilla (11); N Wilcken, Westmead Hospital, Westmead (11); R Epelbaum, Rambam Medical Center, Haifa (11); L Crocchiatti, Ospedale Civile S. Maria Misericordia, Udine (11); U Cirkel, Klinikum Minden, Minden (11); C Gonzalez De Leon, Centro Medico Mugerza, (11); E Rechberger, A. Oe. Kh Der Barmherzigen Schwestern, Linz (11); F Puglisi, Policlinico Universitario, Udine (11); J Keckstein, Lkh Villach, Villach (11); R Rosso, Istituto Nazionale per La Ricerca sul Cancro Oncologia Medica A, Genova (11); H Wiebringhaus, St. Barbara Klinikum, Hamm (11); T Sirisinha, Ramathibodi Hospital, Bangkok (11); L Lundgren, Lund University Hospital, Lund (11); W Aulitzky, Robert-Bosch-Krankenhaus, Stuttgart (11); E Simoncini, Azienda Ospedaliera Spedali Civili, Brescia (11); E Kubista, Akh Univ. Kliniken Wien, Wien (11); A Tulusan, Klinikum Bayreuth, Bayreuth (11); A Contu, Ospedale Civile, Sassari (11); P Papaldo, Istituto Regina Elena, Roma (11); J Thaler, A. Oe. Kh Der Barmherzigen Schwestern, Wels (10); O Campos, Maternidade Byssaia Barreto, Coimbra (10); I Vergote, Uz Gasthuisberg, Leuven (10); S Morales,

Hospital Arnau De Vilanova, Lleida (10); V Chissov, P.A. Herzen Oncological Institute, Moscow (10); E Abdi, Toowoomba Base Hospital, Toowoomba (10); S Ellard, BCCA - Cancer Center Southern Interior, Kelowna (10); B Ojeda, Hospital Santa Creu I Sant Pau, Barcelona (10); M Stauch, Praxis Fuer Haematologie Und Internistische Onkologie, Kronach (10); M Ewertz, Aalborg Sygehus, Aalborg (10); K Moskovits, Szent Imre Hospital, Budapest (10); N Davidson, Broomfield Hospital, Chelmsford (10); C Blomqvist, Akademiska Sjukhuset, Uppsala (10); P Ellis, Guy's Hospital, London (10); L Thurzo, University Of Szeged, Szeged (10); H Meden, Diakoniekrankenhaus, Rotenburg-Wuemme (10); M Kirschbaum, Caritas Kilinik St. Theresia, Saarbruecken (10); J Joffe, Huddersfield Royal Infirmary, Huddersfield (10); M Dank, Semmelweis University, Budapest (10); J Singer, St Margaret's Hospital, Epping (10); P Ruff, Johannesburg Hospital - University Of The Witwatersrand, Johannesburg (10); K Moeller, Herning Centralsygehus, Herning (10); H Redmond, Cork University Hospital, Cork (10); C Rochlitz, Kantonsspital Basel, Basel (9); S Ackland, Newcastle Mater Hospital, Newcastle, New South Wales (9); M Gonzalez-Baron, Hospital La Paz, Madrid (9); A Cheirsilpa, National Cancer Institute Of Thailand, Bangkok (9); D Ten Bokkel Huinink, Diakonessenhuis Utrecht, Utrecht (9); L Perez Michel, Centro Medico Del Noroeste - Imss, Ciudad Obregon (9); O Camara, Friedrich-Schiller-Universitaet, Jena (9); A Santoro, Istituto Clinico Humanitas, Rozzano (9); J Gapski, Trillium Health Centre, Mississauga Site, Mississauga (9); R Lugo Quintana, Hospital Clinica Del Parque, Chihuahua (9); P Barrett-Lee, Velindre Hospital, Cardiff (9); M Stierer, Hanuschkrankenhaus, Wien (9); A Anton Torres, Hospital Universitario Miguel Servet, Zaragoza (9); S Stemmer, Rabin, Petach Tikva (9); G Van Hazel, Mount Hospital, Perth (9); M Gil I Gil, Instituto Catalan D' Oncologia, Barcelona (9); MA De La Cruz, Hospital Virgen De La Salud, Toledo (9); J Hansen, Centrallasarettet, Vasteras (9); L Chow, Queen Mary Hospital, Hong Kong (9); A Hutcheon, Aberdeen Royal Infirmary, Aberdeen (9); A Majlis, Fundacion Arturo Lopez Perez, Santiago (8); H Fujii, Tochigi Cancer Center, Tochigi (8); Y Fujiwara, National Cancer Center Hospital At Tokyo, Tokyo (8); M Donadio, Ospedale S. Giovanni Battista, Torino (8); R Coleman, Weston Park Hospital, Sheffield (8); M Hartmann, Ev. Krankenhaus, Koeln (8); V Heyl, Asklepois Paulinenklinik, Wiesbaden (8); J Bayo Calero, Hospital

Juan Ramon Jimenez, Huelva (8); G Morgan-Villela, Hospital De Especialidades, Guadalajara (8); E Lokkevik, The Norwegian Radium Hospital Montebello, Oslo (8); G Cavazzini, Ospedale Civile Carlo Poma, Mantova (8); F Boyle, The Mater Private Hospital, North Sydney (8); C Tsao, National Cheng Kung University Hospital, Tainan (8); N Niederle, Klinikum Leverkusen, Leverkusen (8); K Gregory, Salisbury District General Hospital, Salisbury (8); S Zheng, 2nd Affiliated Hospital, Zhejiang University, Cancer Institute, Hang Zhou, Zhejiang (8); P Schmidt-Rohde, Allgem. Krankenhaus Barmbek, (8); S Monfardini, Ospedale Busonera, Padova (8); F Coppola, Hospital Aleman De Buenos Aires, Buenos Aires (8); P Manente, Presidio Ospedaliero - Usl 13, Castelfranco Veneto (8); M Constenla Figueiras, Complejo Hospital Ario De Pontevedra, Pontevedra (8); J Mansi, St George's Hospital Medical School, London (8); B Walley, Tom Baker Cancer Centre, Calgary (8); J Schueller, Krankenanstalt Rudolfstiftung, Wien (8); M Clerico, Ospedale Degli Infermi Di Biella, Biella (8); W Eiermann, Frauenklinik Vom Roten Kreuz, Muenchen (8); B Norris, BCCA-Fraser Valley Cancer Centre, Surrey (8); M Crump, Princess Margaret Hospital, Toronto (8); Cm Schlotter, Oekomen. Krankenhaus, Ibbenbueren (8); G Barsanti, Ospedale Campo Di Marte, Lucca (8); C Soto Collins, Clinica De Especialidades No. 30 "Dr. Humberto Torres Sangines", Mexicali (7); X Guang-Wei, Peking University School Of Oncology, Beijing (7); B Nisenbaum, Meir Hospital, Kfar Saba (7); J Grasshoff, Klinikum Quedlinburg, Quedlinburg (7); A Frassoldati, Azienda Ospedaliera Policlinico Di Modena, Modena (7); P Francis, Peter MacCallum Cancer Institute, Melbourne (7); C Underhill, Border Medical Oncology, Wodonga (7); A Wischnik, Zentralklinikum Augsburg, Augsburg (7); R Snyder, St. Vincent's Hospital, Medical Oncology, Melbourne (7); F Melchert, Klinikum Der Stadt Mannheim, Mannheim (7); J Castellanos Diez, Complejo Hospitalario Xeral Cies, Vigo (7); D Elling, Oskar-Ziethen-Krankenhaus, Berlin (7); J Cassinello Espinosa, Hospital General De Guadalajara, Guadalajara (7); R Leonard, Singleton Hospital, Swansea (7); C Poole, Cancer Research UK Trials Unit, Institute For Cancer Studies, Birmingham (7); J Cuevas Sanz, Hospital De La Ribera, Alzira (7); V Bernstein, Vancouver Island Cancer Center, Victoria (7); W Kuhn, Universitaetskliniken Bonn, Bonn (7); G Gasparini, Azienda Complesso Ospedaliero S. Filippo Neri, Roma (7); G Mustacchi, Azienda Ospedaliera Triestina, Trieste (7);

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We are grateful to the members of the Independent Data Monitoring Committee: D Hayes, Breast Oncology Program, University of Michigan Comprehensive Cancer Center, Ann Arbor, Michigan; J Garber, Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts; A Howell, Department of Medical Oncology, Christie Hospital, Manchester; S Lagakos, Department of Biostatistics, Harvard School of Public Health, Boston, Massachusetts; M Picard, Cardiology Division, Massachusetts

General Hospital, Boston, Massachusetts; C Seiler, Department of Cardiology, University Hospital, Swiss Cardiovascular Center, Bern and a patient representative (physician in internal medicine) from Goeteborg.

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